ACTA RADIOLOGICA

Condita a Gösta Forssell

Edita Iussu Societatum Radiologicarum Daniae Fenniae Norvegiae et Sueciae

Indices

Vol. 55 January—June 1961

Contents of Volume 55

CONTENTS OF VOLUME 55

ACTA RADIOLOGICA

EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE NORVEGIAE ET SUECIAE

VOL. 55 JANUARY 1961 FASC. 1

INFLUENCE OF NALORPHINE ON THE SPHINCTER OF ODDI STUDIED BY ROENTGENCINEMATOGRAPHY

by

PERCY LINDGREN and GEORG FREDRIK SALTZMAN

It has long been known that morphine increases the tone of unstriated intestinal muscle in general and hence that of the sphincter of Oddi as well. Most substances belonging to the morphine group, both natural and synthetic, are considered to exercise a similar influence on unstriated muscle. Nalorphine (N-allylnormorphine) (WINTER et coll. 1954) forms an exception in this respect since it is considered that this substance has an antagonistic effect on the tonic action of morphine (HART and MCCAWLEY 1944).

During the last few years we have studied the influence of various drugs upon the sphincter of Oddi by means of a system consisting of an image intensifier and a film camera adapted for roentgencinematography. Nalorphine has also come in for attention in this connection, and as our results diverge in certain respects from the view generally held we considered they were worth placing on record.

Our knowledge regarding nalorphine as a morphine antagonist is mainly based on experimental and clinical experience with this substance in morphine

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intoxication (UNNA 1943, WOODS 1956, FRASER 1957). In general the drug behaves as a narcotic antagonist in the presence of a strong narcotic effect, in the absence of a narcotic effect it behaves as a narcotic, in the presence of narcotic addition it produces withdrawal symptoms. The best known effect of nalorphine is its power to counteract the respiratory depression produced by morphine. The precise mode of action is unknown, although pharmacologic observations suggest that it can best be explained as competitive inhibition.

Nalorphine is said to antagonize intestinal morphine spasm as well as acting as a spasmolytic. HART and MCCAWLEY (1944) observed that in non anaesthetized dogs nalorphine caused a decrease in tone with a slight increase in activity. When morphine was given first the intestinal tone fell to below the starting level while at the same time a certain degree of hyperactivity was noted. When morphine was administered after nalorphine the morphine spasm was not completely inhibited. Similar results were reported by GRUBER and GRUBER (1953), who found that nalorphine will prevent or antagonize the increase in intestinal tone produced by morphine and the series of drugs of the morphine group.

WINTER et coll. (1954) tested the antispasmodic activity of nalorphine on the isolated ileum of the guinea pig and rabbit. As compared with papaverine nalorphine has a very weak antispasmodic activity.

Nalorphine has also been reported to produce an inhibition of gastric and intestinal motility in man (BEAL and SCHAPIRO 1953). In another publication the same investigators (SCHAPIRO and BEAL 1953) made a direct study of the effect of nalorphine on the choledochal sphincter action. When nalorphine was given after the increase in intraductal pressure produced by morphine there was a prompt decrease in common duct pressure, when the nalorphine was administered before the morphine, the characteristic rise in intraductal pressure was not produced.

To sum up, it may be said that according to the results reported in the literature nalorphine has a weak, although distinct spasmolytic effect on unstriated intestinal muscle and displays antagonism not only to the central but also to the peripheral effects produced by morphine.

Material and Methods

The effect of nalorphine on the sphincter of Oddi has been studied in 10 cases. The examinations were carried out in connection with postoperative so called secondary cholangiographies in patients who had undergone cholecystectomy about 5 days previously. The 10 cases were taken in unbroken succession and without selection, from the routine material at Serafimerlasarettet.

The contrast medium used was Hypaque 45 % (sodium diatrizoate) diluted with an equal amount of physiologic salt solution The medium was injected through a rubber tube which had been introduced into the ductus choledochus at the operation An amount of 5 ml of contrast medium was given at each injection the first dose being injected before the nalorphine medication Immediately after the first injection the patient received 10 mg of nalorphine subcutaneously Subsequent injections of contrast medium were carried out at 5 10 15 and 20 minutes after the nalorphine injection Using an Arriflex camera adapted for roentgencinematography and connected to a Philips image intensifier the region of the sphincter of Oddi was filmed for 10 to 20 seconds at an exposure rate of 16 films per second immediately after the conclusion of the respective contrast injections The patient lay in the same position during the whole of the time Following these film recordings 2 to 4 drops of nitroglycerine were administered sublingually and the region of the sphincter of Oddi was filmed 1 and 2 minutes after the administration In addition to these 10 cases a further 3 examinations were carried out in connection with this study These 3 patients first received 10 mg of morphine subcutaneously and were kept under fluoroscopic observation till a constant contraction had arisen in the sphincter of Oddi as soon as this had been established they were given 10 mg of nalorphine Films were then exposed at short intervals for 15 to 20 minutes after the injection of contrast medium

Results

In none of our cases did the first injection of contrast medium carried out before the nalorphine injection cause any demonstrable spasm in the sphincter of Oddi and our experience is thus the opposite of that reported by JACOBSSON et coll (1959) These investigators held that the sudden pressure increase produced by the injection of contrast medium may provoke a rapidly disappearing or more longstanding increase in the tone of the sphincter muscles In all of our cases the medium passed out freely into the duodenum after the first injection and in all 10 cases the bile ducts were found to be completely free from contrast medium at the fluoroscopic examination preceding the next injection of the medium

For the assessment of the reaction of the sphincter of Oddi to nalorphine contractions in the sphincter region were recorded and the widths of the ductus choledochus before and after nalorphine administration were compared Contraction of the sphincter of Oddi was considered to be present only when no contrast medium could be seen to pass out through the sphincter region into the intestine Thus if the lumen of the sphincter was decreased but still allowed visible passage of contrast medium this was not recorded as a spasm

In the films taken 5 minutes after nalorphine medication a sphincter spasm that remained unchanged during the entire film recording was demonstrated

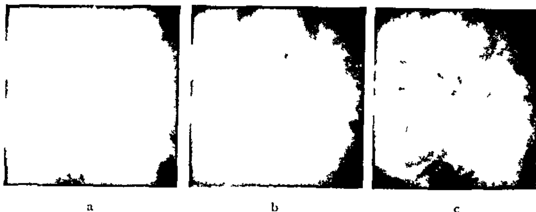


Fig. 1. ♀ 41 years 75 kg. Cholangiography. Effects of nalorphine on the function of the sphincter of Oddi. a) Before nalorphine. Lower part of common duct contrast filled. Good passage of contrast medium to the duodenum. b) 10 minutes after 10 mg of nalorphine subcutaneously. Increased tone of the sphincter. No contrast filling of intramural part of the common duct, no passage to the duodenum. c) 25 minutes after nalorphine, 2 minutes after nitroglycerine. The sphincter is relaxed and allows free passage of contrast medium to the duodenum.

in 3 instances; in these cases no contrast medium passed out into the intestine during the 10 to 20 second period represented in the film. In a further 4 cases contractions of short duration, between each of which contrast medium passed into the intestine, were visible; a noticeable change in the relations of the sphincter had, however, taken place in these cases as compared to the appearances in the film taken before nalorphine medication. In the remaining 3 cases no definite contraction of the sphincter could be observed 5 minutes after the injection of nalorphine.

The situation had changed in the films taken 10 minutes after the administration of nalorphine. In all those cases in which transient spasms had been observed after 5 minutes, a contraction that remained constant during the greater part of the film recording was now apparent. A similarly unchanged contraction was also observed in one of the 3 cases in which no spasm had been demonstrated after 5 minutes; in 2 cases there were still no signs of contraction. Of the 3 cases in which a constant contraction was already present after 5 minutes, 2 still showed an unchanged condition after 10 minutes, while in the third there were now transient spasms with visible passage of contrast medium in the intervals between them.

With regard to the films taken 15 minutes after injection of the nalorphine it was found that the constant sphincter spasm had relaxed in most of the cases although transient contractions were also now seen in most of them. Rapidly recurring but shortlived contractions were visible in the 2 cases without definite spasm after 10 minutes.

Twenty minutes after the administration of nalorphine the contractions had almost entirely ceased in most of the cases, although in a few instances transient spasms were still visible.

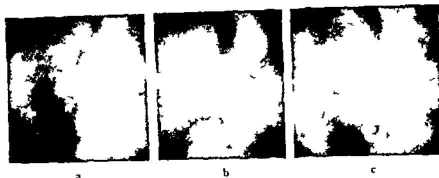


Fig 2 ♀ 66 years 60 kg Cholangiography Effects of nalorphine on the function of the sphincter of Oddi Identical conditions and same results as in fig 1 The concave end of the common duct in (b) indicates a marked spasm in the sphincter and the increased diameter of the duct a higher intraductal pressure

Summing up it may be said that biliary spasm occurred in all 10 cases In 8 cases the contraction remained constant for the greater part of at least one of the 10 to 20 second run of films and in the other 2 cases there were transient spasms that had not been observed before the injection of nalorphine In most cases the sphincteral contraction reached its maximum 5 to 10 minutes after nalorphine had been given although the spasms appeared only at a slightly later stage in a few of the cases The maximal sphincteral contraction lasted for at the most 10 minutes In a few instances it was observed at fluoroscopy that the bile ducts had not lost all contrast medium between two film recordings this was seen only in those cases in which the sphincter spasm had remained constant throughout both film recordings

It should perhaps be stated that the same dose of nalorphine (10 mg) was administered in all 10 cases It would of course have been more correct to work out the dose in relation to the bodyweight of the patients and it may therefore be mentioned that the weight in the cases in which no sphincteral contraction lasting throughout the greater part of a film could be observed constituted the heaviest among the patients (80 and 75 kg) The weight of the other patients varied from 47 to 75 kg

The significance of increased width of the ductus choledochus after morphine medication has been discussed by GUNNARSON (1956) and JONSSON (1960) in connection with intravenous cholegraphy Some difference of opinion has been expressed regarding the diagnostic value of such an increase, but it seems obvious that definite widening must be interpreted as a sign of obstruction to the flow of bile to the intestine On the other hand it also seems probable that not every spasm in the sphincter of Oddi need cause widening of the ductus choledochus

Because of the difficulties experienced in a few cases in obtaining fully satisfactory measurements with the coarse grained film necessitated by the

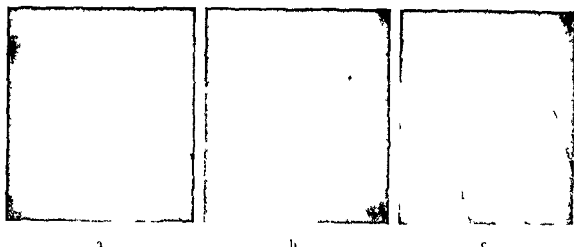


Fig. 3. ♂, 12 years, 37 kg. Cholangiography. Effect of morphine on the sphincter of Oddi. Morphine antagonistic effect of nalorphine. a) Before morphine. Free passage of contrast medium. b) 10 minutes after 10 mg of morphine subcutaneously. Marked spasm of the sphincter. c) 25 minutes after morphine and 10 minutes after 10 mg of nalorphine subcutaneously. Normal conditions seem to have been restored: free passage to the duodenum.

relatively rapid rate of exposure, it was not possible to make exact measurements of the width of the ductus choledochus. Only an unequivocal widening could be recorded as such. Other information may be obtained from Fig. 2. Definite widening of the duct was demonstrated in 7 of the 10 cases, in 2 it was already manifest 5 minutes after the nalorphine injection, in 4 after 10 minutes, and in the seventh 15 minutes afterwards; in no case was such widening seen before a sphincter contraction had been observed. There was no definite evidence of widening in 3 cases. No obvious relationship between widening of the duct and the bodyweight of the patient could be established.

Following nitroglycerine medication, free passage of the contrast medium from the ductus choledochus to the duodenum was observed after 1 minute in every case. In a few instances passage appeared to be free even before the nitroglycerine was given, however. According to our observations the duct in the sphincter region in most instances seemed distinctly wider after nitroglycerine than before the nalorphine medication.

The clinical symptoms and signs could not be recorded in detail in these investigations. Seven of the 10 patients reported that they felt sleepy or dizzy. The size of the pupils was checked in all cases: in 5 of the 10 patients the pupils were much smaller 15 minutes after the nalorphine injection than before it, when examined under the same light conditions.

Sphincter contractions of long duration were rapidly obtained in 2 of the 3 cases in which 10 mg of morphine subcutaneously were given first. In the third case shortlived but frequent contractions were observed in the sphincter of Oddi.

No sphincter contracting effect was observed in these cases from the use of nalorphine Five minutes after the patients had received 10 mg of nal orphine it was no longer possible to distinguish any contraction of the sphincter of Oddi, and the sphincter region was of the same appearance as before the morphine medication

Although it cannot be asserted with ab olute certainty that nalorphine counteracted the action of morphine on the unstriated muscle in these cases seeing that we are not quite sure when the morphine effect had decreased spontaneously it is nevertheless clear that the drug did not in these cases cause a contraction of the sphincter such as was demonstrated in all those cases in which nalorphine had been given without preceding morphine medica tion It is also obvious that nalorphine did not accentuate the spasmogenic effect of the morphine

Discussion

Our results which imply tonic contraction of the sphincter of Oddi after the administration of nalorphine would appear to contradict the commonly held view regarding the action of this drug on unstriated muscle The first question that arises is whether our experimental technique may have in fluenced the result The injection of contrast medium seems to be the only unphysiologic factor in our examination method The effect of the pressure increase following the injection has already been mentioned and it was maintained in that connection that the control injections *before the* ad ministration of nalorphine did not produce any sphincteral spasm to cause obstruction to the outflow The contrast medium used sodium diatrizoate, is relatively pharmacologically inert and can hardly have played any *part in* producing the sphincter spasm recorded after the nalorphine medication The film technique also allows recording of the choledochous function directly after the injection of contrast medium

SCHAPIRO and BEAL (1953) who seem to be the only investigators to have previously studied the effect of nalorphine on *the choledochal* sphincter in man examined as we did, patients who had undergone choledochostomy They employed a different examination technique, however and recorded the common duct pressure The main purpose of their investigation was however to study any interaction that might exist between nalorphine and morphine only in 3 cases were the effects of nalorphine *in themselves* given attention According to these authors curves 5 mg of nalorphine intravenously did not produce any change neither an increase nor decrease in intraductal pres sure It is to be noted however that this dose almost completely blocked the action of a subsequent dose of morphine (10 mg intravenously) In the present investigation 10 mg of *nalorphine* were given subcutaneously but whether this was the explanation of the slightly different results is difficult to say Although our technique did not permit a study of the intraductal pres

sure it seems obvious to us that a tonic sphincter spasm such as we recorded ought to have produced a rise in pressure. The considerable widening of the common bile duct that we recorded in several instances was in all probability a sign of a pressure increase.

The majority of investigations on the effect of nalorphine on unstriated muscle have not been concerned with the sphincter of Oddi but with the recording of the intraluminal pressure and the peristalsis of other intestinal muscles. Two papers in particular are of interest in this connection, both of them reported decreased intestinal tone after nalorphine. HART and McCAWLEY (1944) used dogs and gave 0.5 mg/kg intravenously, and BEAL and SCHAPIRO (1953) studied the intestinal motility in man after 5 mg/kg. Although the sphincter of Oddi and other intestinal muscles usually react in a uniform manner to drugs certain observations have suggested that the choledochal sphincter is capable of action independent of the duodenal musculature (SMITH et coll. 1952). For this reason it is difficult to make any comparisons between our results and these earlier observations of the intestinal motility, and they need not necessarily be considered contradictory.

As opposed to our results regarding the auto effect of nalorphine on the sphincter of Oddi our study of the morphine antagonism has confirmed earlier reports as to a spasmolytic effect (SCHAPIRO and BEAL 1953, ADELMAN and ROSENTHAL 1958, ALPER and VANDAM 1959). Thus on the one hand nalorphine produces a spasm of the unstriated muscle of the sphincter and on the other has the power to counteract spasm produced by morphine. Before this question can be discussed it would seem necessary to obtain an insight into the effect of nalorphine on other organs and functions.

The best known effect of nalorphine is its capacity in counteracting any respiratory depression produced by morphine. This effect becomes apparent only when the depression is considerable, in other words after the administration of relatively large doses of morphine (FRASER et coll. 1956). In these cases a small dose of nalorphine rapidly restores the respiration to — as far as can be judged — a normal level. On the other hand nalorphine produces in an untreated patient a respiratory depression that may be as severe as that occurring after morphine (FRASER et coll. 1956, HUGGINS et coll. 1957). The same is the case with certain other C. N. S. effects, such as miosis. The explanation of this, according to FRASER et coll., would seem to be a molecular competition between nalorphine and morphine for a cellular receptor site. Both drugs apparently have the same effect, qualitatively speaking but nalorphine has a considerably greater affinity. Similar opinions as to a competition have been advanced by other authors (e. g. WINTER et coll. 1954).

Our results would seem to indicate a like mode of action with respect to the effect of nalorphine on unstriated muscle. When given alone, nalorphine seems to be bound to certain cell receptors, its effects resembling those of morphine. When nalorphine is administered to patients previously given

morphine nalorphine competes more successfully than morphine for a site in the cell The marked sphincter spasm due to morphine might thus be replaced by a weaker tone due to nalorphine and the effect could be considered as antagonistic It is possible that smooth muscle needs stronger stimuli to maintain a spasm than to evoke it (an attempt to explain the different effects of the same doses of nalorphine) However before being taken for granted the hypothesis needs support from further investigations and the establishment of proper dose response relationships

Hence our observations would support the theory that nalorphine has a uniform mode of action both in its central and peripheral effects in other words that in all essentials it possesses morphine like properties but with quantitative differences in its effects, because of a greater affinity for some hypothetical receptor site nalorphine acquires an apparently morphine antagonistic action

To characterize nalorphine as a spasmolytic appears to us immaterial and probably has no applicability in intestinal or biliary spasm Nor do we share the enthusiasm of ADELMAN and ROSENTHAL (1958) in using nalorphine as the agent of choice in the treatment of narcotic induced spasm In the latter cases as well true spasmolytics such as amyl nitrite, nitroglycerine and theophylline would appear to be preferable

Conclusions

1 Nalorphine in a subcutaneous dose of 10 mg produced increased tone of the sphincter of Oddi in all 10 cases examined, marked spasm was demonstrated in 8 cases The maximum effect was noted after 5 to 10 minutes

2 The nalorphine spasm was effectively relaxed by 2 to 4 drops of nitroglycerine given sublingually

3 Nalorphine has a distinctly morphine antagonistic effect since 10 mg of nalorphine counteracted and inhibited a spasm in the sphincter of Oddi produced by 10 mg of morphine

4 The results support the hypothesis that nalorphine and morphine have the same qualitative action not only on the central nervous system but also on unstriated muscle cells The tonicizing effect of nalorphine is weaker than that of morphine but as it probably has a greater affinity for the receptor site it competes favourably with morphine The result will appear as a relative spasmolysis This hypothesis is in complete analogy with the current view regarding the mode of action of nalorphine on the central nervous system

5 Nalorphine should not be termed a spasmolytic Its practical value as a means of counteracting narcotic induced intestinal spasm may be said to be inconsiderable

SUMMARY

The function of the sphincter of Oddi was studied with the aid of roentgencinematography in 10 patients undergoing postoperative cholangiography A subcutaneous injection of 10 mg nalorphine produced increased sphincter tone (spasm) in every case This is opposed to certain earlier reports in which spasmolytic properties were attributed to nalorphine When 10 mg morphine were given first nalorphine counteracted the morphine spasm as other investigators have also observed

ZUSAMMENFASSUNG

Die Funktion des sphincter Oddi wurde mit Hilfe der Rontgencinematographie 10 Patienten die sich einer postoperativen Cholangiographie unterzogen hatten studiert Eine sc Injektion von 10 mg Nalorphin erzeugte in allen Fallen eine Erhohung des Sphinktertonus (Spasmus) Dies steht im Gegensatz zu gewissen fruheren Berichten in denen dem Nalorphin spasmolytische Eigenschaften zugeschrieben worden waren Nach Vorbehandlung mit 10 mg Morphin wirkte Nalorphin dem Sphinkterspasmus entgegen wie bereits andere Untersucher beobachtet haben

RÉSUMÉ

La fonction du sphincter d Oddi a eté étudiée par radiocinematographie chez 10 malades au cours de cholangiographies post operatoires L injection sous cutanée de 10 mg de nalorphine a augmenté la tonicité du sphincter (spasme) dans tous les cas Ceci est en contradiction avec certaines publications antérieures dans lesquelles on attribuait des propriétés spasmolytiques a la nalorphine Si on a administré d abord 10 mg de morphine la nalorphine supprime le spasme morphinique comme l ont observé d autres auteurs

REFERENCES

ADELMAN M H and ROSENTHAL A I Nalorphine in the treatment of morphine induced biliary colic J M Sinai Hosp 25 (1958) 36

ALPER M H and VANDAM L D Morphine biliary spasm and nalorphine Anaesthesia 20 (1959) 713

BEAL J M and SCHAPIRO H Effect of N allylnormorphine on gastrointestinal motility Surgery 33 (1953) 65

FRASER H F Human pharmacology and clinical uses of nalorphine (N allylnormorphine) Med Clin N Amer 41 (1957) 393

— VAN HORN G D and ISBELL H Studies on N allylnormorphine in man antagonism to morphine and heroin and effects of mixtures of N allylnormorphine and morphine Amer J med Sci 231 (1956) 1

GRUBER JR C M and GRUBER C M N allylnormorphine as an antagonist to the intestinal spasm produced by the addicting analgesics J Pharmacol exp Ther 109 (1953) 157

GUNNARSON E The bile ducts of cholecystectomised patients with and without dyskinesia before and after morphine injection Acta radiol 45 (1956) 298

HART E R and MCCAWLEY E L The pharmacology of N allylnormorphine as compared with morphine J Pharmacol exp Ther 82 (1944) 339

HUGGINS R A SPENCER W A GEDDES L A et coll Respiratory functions in man following intravenous administration of morphine N allylnormorphine and N allylnormorphine after morphine Arch int Pharmacodyn 111 (1957) 275

JACOBSSON B LANNER, L O and RADBERG C The dynamic variability of the choledocho pancreatico-duodenal junction A roentgen cinematographic investigation Acta radiol 5? (1959) 269
JONSSON M Width of common bile duct before and after morphine studied by cholegraphy Acta radiol 54 (1960) 345
SCHAPIRO H and BEAL, J M The effect of N allylnormorphine on the choledochal sphincter action Surgery 34 (1953) 870
SMITH J L WALTERS R L and BEAL J M A study of choledochal sphincter action Gastroenterology 20 (195?) 129
UNNA K Antagonistic effect of N allylnormorphine upon morphine J Pharmacol exp Ther 79 (1943) ?7
WINTER C A ORAHOVATS P D FLATAKER L et coll Studies on the pharmacology of N allylnormorphine J Pharmacol 111 (1954) 15?
WOODS L A The pharmacology of nalorphine (N allylnormorphine) Pharmacol Rev 8 (1956) 175

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ANGIOGRAPHY OF ANEURYSMAL BONE CYST

by

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The roentgenographic appearances of an aneurysmal bone cyst have often been described in recent years and are generally regarded as characteristic (JAFFE, and SHERMAN & SOONG). A ballooned out distention of the periosteum is usually outlined by a paper thin subperiosteal shell of bone under which an eccentric destruction of both the cortex and the cancellous bone is evident.

The angiographic picture of this lesion has not been described in detail. SCHOBINGER et coll. reported arteriography of an aneurysmal bone cyst in a tibia. They found no changes in the arteries. During the venous phase, however, there was diffuse opacity of the cystic areas and the contrast medium was retained in the vessels of the involved area. The histologic appearances of the large distended or distorted thin walled blood spaces in these lesions were described by JAFFE. He believed that the blood in these vascular spaces is not stagnant and that the large blood pool is being steadily drained and replenished. We have performed angiography of three aneurysmal bone cysts and these have shown uniform appearances. Some characteristic features have been observed.

The distal part of the femoral shaft of a 28 year old man was involved in the first case (Fig. 1). In the second, the proximal metaphysis of a tibia of

Submitted for publication 25 July 1960.



Fig 1 Aneurysmal bone cyst in distal part of femoral shaft of man aged 28 a) Cyst surrounded by a thin shell of bone b) Angiography early arterial phase Arteries leading to lesion contrast filled further peripherally than other arteries c) Late arterial phase Patchy opacity of cyst d) Venous phase Veins draining cyst contrast filled

a 13 year old girl was the site of the lesion (Fig 2) and in the third case the proximal metaphysis of an ulna of a 16 year old girl was affected The femoral cyst was resected and the lesions in the ulna and tibia were curetted

The histologic findings of the tissue from these three cases were typical The loose fibrous tissue that formed part of the specimen was richly vascular and contained a large number of slightly dilated thin walled normal blood vessels Several multinucleated giant cells and thin bands of osteoid were seen Large and small cystic often thin walled blood spaces varying from a few millimeters to several centimeters in diameter were characteristic features (Fig 3) Giant cells were evident on the luminal aspect of the spaces, which they appeared to line Narrow bands of osteoid often formed part of the wall of the blood spaces (Fig 4) In addition osteoid and cancellous bone were sometimes found in the stroma with occasional spotty calcification peripherally The cortical bone beneath the periosteum was attenuated, in some areas the stroma was purely fibrous or contained many giant cells along with osteoid and bone Van Gieson staining of the sections failed to reveal the presence of elastic fibers in the walls of the small and large blood spaces of the lesions

The angiographic examinations were all performed with a serial technique in two of them an automatic changer being used The arteries leading to the lesions were in two of the cases markedly dilated and in the other slightly dilated During the passage of the contrast medium a slight but definite degree of opacity was noted throughout the whole area of the cyst and had



a b

c d e

Fig 2 Aneurysmal bone cyst in proximal metaphysis of tibia of girl aged 13 a) Well delimited eccentric superficial destruction and blown out thin periosteal shell of bone b) Arteriogram in late arterial phase Identical projection as in (a) Opacity of whole cystic area c) d) e) Serial arteriography lateral c) In early arterial phase the arteries feeding the lesion are better filled than other arteries d) In late arterial phase patchy opacity of cyst e) In early venous phase the veins draining the cyst are already well filled indicating an arteriovenous shunt



Fig 3 Lo power photomicrograph of resected aneurysmal bone cyst shown in fg 1 × 6 Great est p t of les onal t sue consists of va cular spa ces f varying ze some of which contain blood res dues Periosteal shell of bone at upper border

Fig 4 Photom crograph of curetted tissue from aneurysmal bone cy t × 200 Loose fibrous tissue with many capillaries and some giant cells Osteo d i wavy wall of collapsed large vascular space

a certain patchy distribution (Figs 1 and 2) There was no peripheral hyper vascularized zone as in malignant tumors The veins leading from the lesion were filled somewhat earlier than the other veins indicating an arteriovenous shunt through the lesions the degree of shunt w is however considerably less than that in most malignant tumors The patchy densities in the cystic area persisted late in the venous phase The increased opacity must be due to the presence of contrast medium in the vascular lumina of the cyst Whether the contrast medium passes through the many small vessels of the fibrous stroma or the large vascular lumina or through both cannot be gathered from the angiograms We feel however that the patchy opacities could be explained by the presence of diluted contrast medium in the large vascular spaces

The roentgenographic appearances of an aneurysmal bone cyst are *in some* cases atypical When the thin blown out shell of bone is absent the roent genographic changes may suggest a malignant tumor Such tumors are, how ever generally hypervascularized especially peripherally Thus *in most in*stances it should be possible to differentiate a malignant tumor e g fibro sarcoma or osteogenic sarcoma, from an aneurysmal bone cyst with the aid

of angiography. In the rare instance when the cyst is found in or adjacent to an epiphyseal region the differentiation from giant cell tumor in the ordinary roentgenogram is difficult. The angiographic appearances of giant cell tumor of bone as described by DOS SANTOS and others are characterized by a homogeneous but not patchy degree of opacity of the tumor area during the passage of the contrast medium through its vessels. The giant cell tumor contains an increased number of capillaries and these are too small to be observed directly in the angiogram. The presence of contrast medium in these vessels, however, causes the diffuse opacity of the tumor tissue. We made a comparison of the angiograms of 5 cases of giant cell tumor of bone with the angiograms of our three cases of aneurysmal bone cyst. In most of the giant cell tumors the opacity was somewhat more intense and more homogeneous than in the cysts. The angiographic appearances of these two different processes were, however, not obviously different in all cases. Angiography cannot therefore be relied upon for the differentiation between these two conditions.

SUMMARY

Angiography of an aneurysmal bone cyst may demonstrate a moderate hypervascularization of the lesion with patchy contrast filling of the cystic area and a moderate arterio venous shunt. Three cases are described and discussed and the differential diagnosis is considered.

ZUSAMMENFASSUNG

Die Angiographie einer aneurysmatischen Knochencyste kann eine mässige Hypervaskularisierung der Erkrankung mit unregelmässiger Kontrastfullung des cystischen Abschnittes und einem massigen arteriovenosen Shunt zeigen. Drei Fälle werden beschrieben und diskutiert, die Differentialdiagnose wird besprochen.

RÉSUMÉ

L'angiographie d'un kyste anévrismal osseux peut montrer une hypervascularisation modérée de la lésion avec opacification en taches de la région kystique et shunt artério-veineux modéré. Les auteurs en présentent et en étudient trois cas et examinent le diagnostic différentiel.

REFERENCES

DOS SANTOS, R.: Arteriography in bone tumors. J. Bone Jt Surg. 32 B (1950), 17.
JAFFE, HENRY L.: Tumors and tumorous conditions of the bones and joints. Lea & Febiger, Philadelphia 1958.
SCHOBINGER, R. and STOLL, H. C.: The arteriographic picture of benign bone lesions containing giant cells. J. Bone Jt Surg. 39 A (1957), 953.
SHERMAN, R. S. and SOONG, K. Y.: Aneurysmal bone cyst. Its roentgen diagnosis. Radiology 68 (1957), 54.

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RENAL OSTEONEPHROPATHY

by

STEN CRONQVIST

Renal osteonephropathy is a term used to describe skeletal changes sometimes seen in association with renal disease. The conditions of this disease may be fundamentally different. The most common and therefore most important condition is chronic renal insufficiency resulting from chronic glomerulonephritis, chronic pyelonephritis, or anomalies of the kidney or lower urinary tract. The second type consists of selective tubular disorders (DENT 1952).

The osseous changes are of various types. In the first cases published, represented by children, the osseous changes were regarded as rachitic and the term "renal rickets" was used to define the condition (LUCAS 1883). Some of the cases were accompanied by dwarfism and sexual infantilism and were classified as renal dwarfism or renal infantilism (FLETSCHER 1911, BARBER 1920).

The roentgen findings in *renal rickets* were summarized by PARSONS (1927) and later by TEAL (1928), who distinguished two roentgenologic types, a rachitic and a "woolly" type. In the former the changes were considered identical with those of rickets, in the latter they were thought to be characteristic of renal infantilism. In these cases the trabeculae of the bone were irregularly

Submitted for publication 13 June 1960.

thickened and poorly defined and the ossification was uneven which according to the authors gave the bone a stippled, woolly appearance Alterations of this kind were observed in the advanced cases in which the bones were also deformed

In one of TEAL'S cases there was cortical erosion, which was regarded as constituting 'the most important feature in the radiographic appearance from a diagnostic point of view

NICHOLS & SHIFLETT (1934), in contrast to TEAL, claimed that the roentgen appearance of renal rachitis is not pathognomonic Later reports began to appear of osseous changes in adults with chronic renal insufficiency, and the osseous alterations were found to coincide with those seen in osteitis fibrosa cystica In advanced cases the roentgenographic appearance was identical with that of hyperparathyroidism, and the disease was called renal osteitis fibrosa generalisata or renal hyperparathyroidism (ALBRIGHT)

Skeletal changes Two types of roentgen changes can thus be distinguished one in which the lesions resemble those seen in rickets and one in which they resemble those of osteitis fibrosa cystica generalisata (SUSSMAN et coll 1942) The former type occurs before, the latter mainly after, closure of the epiphyseal line Occasionally both types may be found in the same patient Ignorance of the possibility of this concurrence has been held responsible for the confusion in the interpretation of the roentgenographic appearance of renal osteodystrophy, particularly in children (DENT & HODSON 1954)

Before closure of the epiphyseal line the lesions are limited mainly to the distal part of the long bones, especially the radius and the ulna, where the metaphyses are increased in width, cupped, and of irregular outline (Fig 10) In more advanced cases there is general rarefaction, obliteration of all compact tissue, and coarsening of the trabeculae in the cancellous bone These changes may also occur in the skull, with granular rarefaction and splitting of the lamina interna and lamina externa, sometimes with thickening of the bone (Fig 1) Deformation of the lower limbs may also occur, due either to 'softness of the skeleton or possibly to epiphyseolysis, at times resulting in dwarfism (BRAILSFORD 1933)

A generalized or granular decalcification with or without disarrangement of the trabeculae may also be seen in adults, i e after closure of the epiphyseal line Osteoporosis is described particularly in the older literature as a salient finding Subperiosteal erosion is common and readily recognized As mentioned this erosion was considered by TEAL as an important diagnostic criterion of renal rickets, but CAMP & OCHSNER (1931) stressed the occurrence of the same type of change in hyperparathyroidism Such erosion has since often been described in hyperparathyroidism and in renal osteodystrophy (PUGH 1951, GLASGOW et coll 1955, DENT and HODSON 1954) The change is most frequently located in the middle phalanges of the fingers (Figs 2 and 5) but also occurs



Fig 1 Alternating sclerosis and rarefaction of skull Calcification in the wall of the carotid siphon Patient aged 34



Fig 2 Subperiosteal cortical erosion most marked in middle phalanges Bone trabeculation altered Small cysts in distal end of third metacarpal bone

in the medial part of the upper third of the tibia in the corresponding parts of the humerus and femur in the acromion and lateral end of the clavicle and the distal part of the ulna (Fig 3) Roentgenologically it is seen as a rarefaction with a spicule like arrangement of the cortex (Fig 3c)

Resorption of the lamina dura (Fig 4) and occasionally though rarely of the distal phalanges of the fingers has also been described (Fig 5) In advanced cases published in recent years the roentgen appearance was dominated by osteosclerosis (CRAWFORD et coll 1954 BAKER 1954 BROOKFIELD et coll 1955) The sclerosis may involve the major part of the skeleton but it is most frequently localized to and most easily recognized in the spine, particularly the lumbar spine Sometimes a whole vertebra is sclerotic while in other cases the sclerosis is present in broad zones adjacent to the superior and inferior surfaces of the body Sometimes it is patchy, the alterations then contrasting sharply with the contiguous normal or even rarefied bone The changes are often seen in the entire spine but they may also be localized to a single vertebra (Fig 6)

Metastatic calcification Roentgen examination will sometimes also show calcification of soft tissue in various regions — metastatic calcifications (HUBBARD 1920 ANDERSEN et coll 1942 MULLIGAN 1947 PENDERGRASS 1954) Three types have been distinguished a physiologic, a vascular and a 'pathologic' In the physiologic type the calcium appears at those sites where acidotic excretion normally occurs — such as lungs stomach kidney The vascular calcifications are present not only in the larger arteries of the body but may



Fig 3 Subperiosteal cortical erosion of humerus (a) of the upper medial part of the tibia (b) of the *femur (c) and of the lateral end of the clavicle (d)*

also be seen even in the small arteries of the extremities (Figs 5 and 7), which in more advanced cases appear as calcareous tubes Calcifications situated around joints, in the synovia, and in or adjacent to tendinous attachments, are described (Fig 8) According to some authors, such changes occur only in co existing active arthritis As a rule metastatic calcifications occur in the patients with advanced osseous changes, but they may also be the first roentgen sign of renal osteodystrophy

We have had the opportunity of examining a number of cases of chronic renal insufficiency showing osseous changes The kidney diseases were chronic pyelonephritis in 4 cases, chronic glomerulonephritis in 1 case and polycystic kidney disease in 1 case



Fig 4 Lower ja v Ab ence of lamina dura

Case reports

Ca 1 Male aged 17 Proteinuria and isosthenuria had been diagnosed at 8 years Uraemia and severe leg pain at 15 years The N P N was then increased The maximum specific gravity of the urine v as 1 002 He had acidosis with a bicarbonate value of 13 m mol The serum calcium was somewhat below normal the serum phosphorus somewhat above Urea clearance 9 The b carbonate value returned towards normal on special treatment of the acidosis At 17 years the N P N was 200 mg He then had acidosis with a bicarbonate value of 13 8 m mol The serum calcium was 10 mg/100 ml the serum phosphorus 7 mg/100 ml The alkaline phosphatases rose from 29 to 91 units After an infection at 19 years the patient became worse N P N 250 mg ° Acidosis with a bicarbonate value of 53 8 m mol The pat ent died

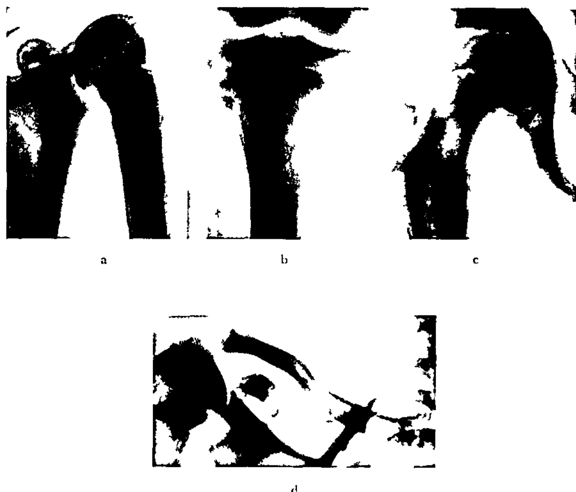
Roentgen exan mation at the age of 17 had revealed small calcifications in both kidneys The entire skeleton was abnormally dense and the trabeculae were thickened and coarse The middle phalanges of the fingers and the medial proximal part of the humerus femur and tibia shov ed marked subcortical rarefaction The epiphyseal lines at the distal ends of the long bones were abnormally v ide and their outline was irregular and diffuse Re examination 2 years later showed a certain regression of the sclerosis in the metaphysis and the epiphyseal lines were no longer so wide or so diffuse (Fig 10)

Autopsy revealed cystic kidneys with several pin sized to hazelnut sized cysts Calcium deposits v ere seen in the tubular epithelium and in the cysts Calcifications were also *present in* the pancreas in sections from the intestine and in the spleen Th vertebral bodies and the sternum showed advanced osteoporosis Between the trabeculae the connective tissue was loose and contained fibroblast like cells

Diag osis Polycystic kidney disease v ith uraemia

The roentgen appearance was dominated by sclerosis Wide spread subperiosteal erosions were seen Changes of the rachitic type responded well to special treatment of acidosis In this case the bone pain was the outstanding symptom

Ca e 2 Female aged 36 At 8 years she had undergone operation with extirpation of the left part of a horseshoe kidney because of hydronephrosis At 22 years hydronephrosis of the right part of that kidney and proteinuria were diagnosed N P N 35 mg/100 ml Specific



a b c

d

Fig 3 Subperiosteal cortical erosion of humerus (a) of the upper medial part of the tibia (b) of the femur (c) and of the lateral end of the clavicle (d)

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We have had the opportunity of examining a number of cases of chronic renal insufficiency showing osseous changes The kidney diseases were chronic pyelonephritis in 4 cases, chronic glomerulonephritis in 1 case and polycystic kidney disease in 1 case



Fig 4 Lower jaw Absence of lam na dura

Case reports

Ca 1 Male aged 17 Proteinuria and isosthenuria had been diagnosed at 8 years Uraemia and severe leg pain at 15 years The N P N was then increased The maximum specific gravity of the urine was 1 007 He had acidosis with a bicarbonate value of 13 m mol The serum cal cium was somewhat below normal the serum phosphorus somewhat above Urea clearance 9 The bicarbonate value returned towards normal on special treatment of the acidosis At 17 years the N P N was 200 mg He then had acidosis with a bicarbonate value of 13 8 m mol The serum calcium was 10 mg/100 ml the serum phosphorus 7 mg/100 ml The alkaline phosphatases rose from 29 to 91 units After an infection at 19 years the patient became worse N P N 250 mg Acidosis with a bicarbonate value of 53 8 m mol The patient died

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Diagnosis Polycystic kidney disease with uraemia

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Fig 5 Resorption of the outer phalanges Subperiosteal erosion of the middle phalange with calcification of small vessels

gravity of urine 1 017 Proteinuria max 0 08 mg/100 ml Five years later joint pain developed The N P N was then 70 mg/100 ml Urea clearance 8 % The following year the chronic renal insufficiency became worse The N P N was 195 mg/100 ml serum calcium 4 5 m Eq serum phosphorus 10 4 mg/100 ml Alkaline phosphatase 13 units The lowest bicarbonate value noted was 12 2 m mol The patient died 36 years old

Roentgen examination in 1955 had revealed widespread calcifications in the arteries of the abdomen and extremities Signs of sclerosis were seen in the lumbar spine and subcortical erosions in phalanges of the hands and feet Right kidney was diminished in size

Autopsy The right kidney showed marked interstitial fibrosis with calcifications Widespread interstitial calcifications were also seen in the lungs Sections from the finger phalanges showed a thin cortex with signs of active bone destruction with numerous osteoclasts and fibrous degeneration of the bone

Diagnosis Chronic pyelonephritis with uraemia

Slight sclerosis and marked subperiosteal erosions were demonstrated particularly in the middle phalanges of the fingers Calcifications were found not only in the arterial walls but also in the kidneys and lungs Joint pain was a prominent feature of the clinical picture

Case 3 Female aged 54 At the age of 48 proteinuria and increased N P N had been diagnosed Specific gravity of urine 1 018 Urea clearance 21 % respectively 18 % During the following years she was repeatedly admitted to hospital In 1951 she was then 51 years the serum calcium was 5 2 m Eq and the serum phosphorus 5 0 mg/100 ml In 1952 the patient complained of joint pain In 1954 the urea clearance was 7 4 % Serum calcium 5 6 m E q Serum phosphorus 6 mg/100 ml Alkaline phosphatase 30 units The N P N gradually rose to about 100 mg/100 ml She had acidosis during the major part of her illness despite continuous treatment The patient died with cardiac insufficiency at the age of 54

Roentgen examination In 1947 the left kidney was small Re examination in 1952 revealed a ureteric stone and changes in the thoracic and lumbar spine with slight rarefaction and coarse trabeculae In 1954 sclerosis along the superior and inferior surfaces of the vertebral bodies was noted Similar changes were seen in other parts of the skeleton Pathologic fractures were demonstrated in the right superior ramus and in the inferior ramus of the ischium Erosions were seen on the medial upper aspect of the tibia

Autopsy revealed small contracted kidneys with chronic pyelonephritis The parathyroid glands were hypertrophic

Diagnosis Chronic pyelonephritis with uraemia

Roentgenologically the lesions increased between 1952 and 1954 There was marked rarefaction and subcortical erosions were demonstrated Acidosis had been present during the



a



b

Fig. 6

a) Lateral view of lumbar vertebral bodies showing sclerosis especially adjacent to the intervertebral discs

b) Post mortem film of vertebral body showing same changes

major part of the disease Autopsy showed severe parathyroid hypertrophy despite absence of more advanced changes of the type of osteitis fibrosa generalisata The patient had also had dull joint pain

Case 4 Male aged 25 At 10 years proteinuria had been diagnosed At 19 years the N P N was moderately increased Specific gravity of urine max 1 014 Protein in urine max 0 5 mg/100 ml At 24 years he had anaemia The N P N was then 100 mg/100 ml He had a swelling in the left sternoclavicular joint and another in the left elbow Biopsy specimens showed changes which were interpreted as metastatic deposition of calcium as a consequence of renal osteodystrophy The following year the swelling increased and subcutaneous well defined infiltrations occurred in different parts of the body surface CO_2 = 50 vol % Serum calcium 12 4 mg/100 ml Serum phosphorus 9 0 mg/100 ml Alkaline phosphatase max 16 units N P N max 258 mg/100 ml The patient died

Roentgen examination In 1953 large calcium masses adjacent to one of the sternoclavicular joints and in the soft tissues at the tip of the olecranon were demonstrated Re examination in 1954 revealed bilateral changes in the medial end of the clavicle Fresh periosteal deposits were demonstrated on the left side The structure in this region showed wide spread destruction alternating with rarefaction The trabeculae were partly eroded and partly sclerotic Erosions were also seen in the ribs The calotte showed rounded sclerotic areas Skeletal changes with rarefaction alternating with sclerosis were generalized and observed in the entire lumbar spine pelvic girdle femur and lower leg A fist-sized expanding process fairly well defined and due to calcium deposits was present in the right pubic region Abundant calcifications were seen in the vessel walls The kidneys were contracted

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Diagnosis Chronic pyelonephritis with uraemia

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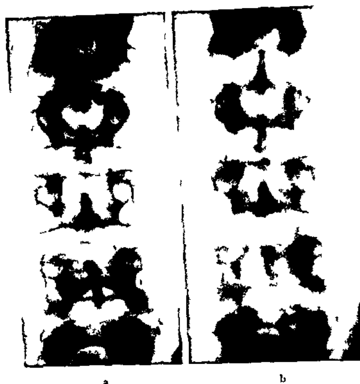


Fig 8 a) Lumbar sp ne without definite os eous chang s b) Three years later General scleros of vert bral bodi

calotte The lamina interna and lamina externa were poorly developed The phalanges showed irregular rarefactions Periosteal erosion was present in the middle phalanges of the fingers and a small cystic swelling in M3 of the left hand Irregular rarefaction was also seen in the femur and humerus on both sides The thoracic and lumbar spine as well as the pelvic girdle showed sclerosis

Diagnosis Chronic pyelonephritis with uraemia

The patient had had proteinuria and renal stone at a fairly earl age She had generalized skeletal changes with a single cyst

Case C Male aged 29 At 17 years the patient had undergone left sided n phrectomy for pyelonephritis with hydronephrosis He had since had repeated attacks of pyelitis and during the following years proteinuria and renal insufficiency with falling clearance N P N about 100 mg/100 ml At 29 years the serum calcium was 3 9 m E q Serum phosphorus 6 0 mg/100 ml bicarbonate value 16 1 m mol N P N 110 mg/100 ml

Roentgen examination In 1955 when the patient was 24 small calcifications were demonstrated in the right kidney which was abnormally small Three years later he showed g neralized sclerosis and subperiosteal erosions in the middle phalanges of the fingers After a further 2 years the sclerosis and the subperiosteal erosions in the fingers had advanced

Diagnosis Chronic pyelonephritis with uraemia



Fig 7 Man aged 25 Extensive calcifications of vessels

Autopsy showed a shrunken right kidney The left kidney was small Calcium deposits were seen in the tubular lumina in some parts of the kidney and in the basal membranes in others All of the parathyroid glands were markedly enlarged The glands were built up mainly of chief cells There was wide spread bony destruction in the form of lacunar resorption The bone trabeculae in the marrow were narrow and eroded by lacunae The bone marrow between the changed trabeculae were fibrous and sometimes the seat of numerous cells of osteoclastic type The vessels showed calcifications

Diagnosis Nephrosclerosis

In this case the history was a long one and the picture dominated by metastatic calcifications Marked skeletal changes were found with erosion and rarefaction alternating with sclerosis Autopsy revealed severe enlargement of all the parathyroid glands which were built up mainly of chief cells

Case 5 Female aged 37 Proteinuria and renal stone had been diagnosed at 22 years The patient had had repeated attacks of pyelitis at 23 She had undergone operation for right renal stone at 24 years and nephrectomy at 25 for stone in the left kidney Between the age of 34 and the age of 36 the N P N varied between 60 and 80 mg/100 ml During that period she complained of increasing stiffness of the legs and lumbar spine

At 37 the N P N was increased and she had isosthenuria Specific gravity of urine 1 007 Urea clearance was 8 % Acidosis with a bicarbonate value of 15 5 m mol The serum calcium was 5 6 m E q Serum phosphorus 1 2 mg/100 ml Alkaline phosphatase 73 units

Roentgen examination In 1954 the patient then 37 had wide spread granular atrophy of the



Fig 8 a) Lumbar spine without definite osseous changes b) Three years later General sclerosis of vertebral bodies

calotte The lamina interna and lamina externa were poorly developed The phalanges showed irregular rarefactions Periosteal erosion was present in the middle phalanges of the fingers and a small cystic swelling in M3 of the left hand Irregular rarefaction was also seen in the femur and humerus on both sides The thoracic and lumbar spine as well as the pelvic girdle showed sclerosis

Diagnosis Chronic pyelonephritis with uraemia

The patient had had proteinuria and renal stone at a fairly early age She had generalized skeletal changes with a single cyst

Case 6 Male aged 29 At 17 years the patient had undergone left sided nephrectomy for pyelonephritis with hydronephrosis He had since had repeated attacks of pyelitis and during the following years proteinuria and renal insufficiency with falling clearance N P N about 100 mg/100 ml At 29 years the serum calcium was 3 9 m E q Serum phosphorus 6 0 mg/100 ml bicarbonate value 16 1 m mol N P N 110 mg/100 ml

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Diagnosis Chronic pyelonephritis with uraemia



Fig 9 Soft tissue calcifications adjacent to elbow joint

Case 7 Male aged 48 At the age of 30 the patient had had chronic glomerulonephritis and in the following years proteinuria In 1955 when 45 he had an acute exacerbation with anuria and the N P N was then 150 mg/100 ml to 200 mg/100 ml He was treated with the artificial kidney on repeated occasions and afterwards improved and when he left hospital the N P N was 60 mg/100 ml He soon complained of fatigue and back ache as well as pain in the shoulders hands feet and knees Serum calcium was 2 8 mg/100 ml Serum phosphorus 7 mg/100 ml bicarbonate 26 8 Four months later he felt worse The N P N was then 108 mg/100 ml Serum calcium 1 9 m E q Alkaline phosphatase was raised The patient died

Roentgen examination In 1955 abnormally small kidneys but no skeletal changes were seen In 1959 the kidneys had contracted still more and the entire spine was sclerotic

Autopsy Small contracted kidneys

Diagnosis Chronic glomerulonephritis

It is generally recognized that chronic renal insufficiency is responsible for the osseous changes but the underlying mechanism is not properly understood A base cannot, for example, be excreted in renal insufficiency, and the result will be acidosis and an increase in the concentration of the phosphate ions in the blood Some authors believe the acidosis to be the direct cause of the skeletal changes (ALBRIGHT et coll 1937) Others however consider that it is the relatively low calcium concentration in relation to the increased amounts of phosphate that prevents normal new bone formation (MITCHELL 1930) It is possible that an acquired vitamin D resistance may also be a contributory factor (STANBURY 1957) Changes in the ratio between the serum calcium and phosphorus have also been described as a cause of increased parathyroid activity with osteitis fibrosa generalisata as a consequence (BERGSTRAND 1921, GILMOUR 1947) Some authors believe that the primary cause of the syndrome, including the renal disease, is hypophyseal dysfunction (CHOWN 1935) It is probable that the skeletal changes are not caused by a single factor but result from the combined effects of two or more An increased parathyroid activity thus may explain the subperiosteal erosion while the acidosis together with a change in the value of serum Ca and serum P may cause the rachitic like changes As mentioned, the type of skeletal changes in a given case generally depends

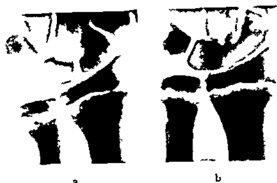


Fig 10 Chronic renal failure for 10 years in man aged 18 Changes of rachitic type a) Epiphyseal line widened and irregular distal part of ulna and radius broadened b) Regression on special treatment of the acidosis.

on the patient's age Whether the severity or type of osseous changes vary with the degree of renal insufficiency is not known It appears however as if even moderate renal insufficiency can with time cause skeletal changes In all of the present cases the patients had a long history of renal disease Raised alkaline phosphatase indicating skeletal destruction was noted in five Acidosis was also noted in four cases The roentgen findings in the author's cases agreed with those described in the literature summarized above

Joint pain and/or stiffness were reported by most patients These symptoms were the indication for roentgen examination in four cases In three cases the pain was dull while in one it was stabbing

In some cases the vertebral changes were detected incidentally in *routine films* of the kidneys or chest and prompted further investigation In two cases the spinal changes were initially slight with generalized rarefaction and irregular coarse trabeculation Roentgen control showed advancing sclerosis and the provisional diagnosis of renal osteonephropathy was confirmed (Fig 9) Similar slight rarefaction has been seen in several cases of chronic renal insufficiency in elderly patients who could not be followed up roentgenologically Senile osteoporosis could not be excluded in these cases However an incidental finding of even moderate osseous changes in patients with chronic renal disease should direct the examiner's thoughts to the possibility of renal osteodystrophy

In the present material the youngest patient was 17 years old A definite diagnosis of renal disease had been made 8 years previously and as expected both types of skeletal changes (rachitic and osteitis fibrosa cystica generalisata) were seen A noteworthy finding in this case was the regression of the rachitic changes after protracted treatment of the acidosis (Fig 10) Such regression has also been described by ALBRIGHT, for example and has been taken as a



Fig 11 Skeletal changes of the Paget type in a case of chronic renal failure

sign that the acidosis is the main cause of the skeletal changes Regression of the subperiosteal erosions after similar therapy has also been described, though no such improvement was observed in the present case

Osteosclerosis of varying severity was seen in most of the cases According to the pathologists a certain degree of sclerosis is regularly seen in patients with renal osteonephropathy — even in the absence of roentgenologically demonstrable sclerosis (GINZLER et coll 1941, JAFFE 1942) This microscopic sclerosis is the result of a reactive new bone formation proceeding together with bone destruction, in the event of an increased rate of new bone formation, e g during remission, the sclerosis may be roentgenologically demonstrable This is also the case in patients receiving intense calcipherol treatment (HOLMAN 1952)

Diagnosis In the introduction it was mentioned that osseous changes may also occur in renal diseases not resulting in renal insufficiency Such renal

diseases are Fanconi Chiari s disease and idiopathic hypercalcaemia and others They are all due to selective disorders of the tubules which are characterized biochemically by low to normal serum calcium low phosphatase and normal or moderately raised phosphate values

From a differential diagnostic point of view primary hyperparathyroidism offers the greatest difficulties In this disease the osseous changes may be of the same nature as in renal osteonephropathy Secondary chronic renal insufficiency due to deposition of calcium in the kidneys or stone formation is not uncommon In primary hyperparathyroidism the serum calcium is raised and the serum phosphate depressed while in renal osteonephropathy the converse changes are said to be most common though by no means the rule In advanced cases of these two diseases the roentgenologic findings as well as the clinical picture may thus be identical and then careful inquiry into the patient s history may help to establish the diagnosis

Osteoporosis, common in elderly patients is also an early roentgenologic sign of renal osteonephropathy In elderly patients with chronic renal insufficiency then it is not always easy to decide the significance of the finding The absence of subperiosteal erosions and normal calcium phosphate values are against renal osteonephropathy

As known the osseous changes in certain stages of hyperparathyroidism renal osteonephropathy and osteitis deformans (Paget) may be similar (LIGHTWOOD 1932 GUTMAN et coll 1938 ANDERSEN et coll 1942) (Fig 11) The further cour e of the roentgen changes as well as the finding of normal serum Ca and serum P together with an excessive rise of the alkaline phosphatase in Paget s disease make a differential diagnosis possible

The roentgen findings may be dominated by metastatic calcifications But such calcifications are no more pathognomonic than the skeletal changes Such changes are also seen in idiopathic hypercalcaemia in Paget s disease in hypervitaminosis D and in this last mentioned condition bone changes resembling osteosclerosis may also occur

In the final diagnosis of renal osteonephropathy in renal insufficiency, then knowledge of the primary nature of the renal disease or of the malformation of the kidney is important Low serum calcium and raised serum phosphate suggest renal osteonephropathy None of the roentgen changes of renal osteonephropathy are pathognomonic but like the metastatic calcification in cases of chronic renal insufficiency osseous changes particularly of the rachitic type should guide the examiner s thoughts to renal osteonephropathy

SUMMARY

Two types of skeletal changes in connection with chronic renal insufficiency each of which appears to have a different pathogenesis are described and discussed An incidental finding of oss ous changes in chest films or conventional films of the abdomen in cases of chronic renal insufficiency is suggestive of renal osteodystrophy



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CUTMAN A B and PARSONS W B Hyperparathyroidism simulating or associated with Paget s disease Amer Int Med 12 (1938) 13
HOLMAN C B Roentgen manifestations of vitamin D intoxication Radiology 5? (1952) 805
HUBBARD R S and WENTWORTH J A A case of metastatic calcification associated with chronic nephritis and hyperplasia of the parathyroids Proc Soc exp Biol 18 (1920—21) 307
JAFFE H L Primary and secondary (renal) hyperparathyroidism S Clin north America 22 (1942) 621
LEVIN R T and GENOVESE D C Report of a case of longstanding renal insufficiency with extensive metastatic calcifications (renal osteitis fibrosa) Amer J Roentgenol 64 (1950) 493
LIGHTWOOD R A case of dwarfism and calcinosis associated with widespread arterial degeneration Arch Dis Childh 7 (1932) 193
LIU S H and CHU H J Studies of calcium and phosphorus metabolism with special reference to pathogenesis and effects of dihydrotachysterol and iron Medicine 22 (1943) 103
LUCAS R C Form of late rickets associated with albuminuria rickets of adolescence Lancet 1883 I p 993
MENVILLE L J WILLIAMSON L and MATTINGLY D Renal rickets with report of a case Radiology 39 (1942) 410
MITCHELL A G Nephrosclerosis in childhood with special reference to renal rickets Amer J Dis Child 40 (1930) 101 345
MULLIGAN R M Metastatic calcification Arch Path 43 (1947 177
NICHOLS B H and SHIFLETT F L Renal rickets with report of case Radiology 23 (1934) 677
PARSONS L G The bone changes occurring in renal and coeliac infantilism and their relationship to rickets Arch Dis Childh 2 (1927) 1
PENDERGRASS E I and BROOKS F P Report of a case of osteonephropathy with vascular calcification in infancy Radiology 62 (1954) 227
PUGH D G Subperiosteal resorption of bone Amer J Roentgenol 66 (1951) 577
STANBURY S W Azotaemic renal osteodystrophy Brit Med Bull 13 (1957 57
SUSSMAN M L and POPPEL M H Renal osteitis Amer J Roentgenol 48 (1942) 726
TEAL C G A radiological study of bone changes in renal infantilism Brit J Radiol 1 (1928 49

ZUSAMMENFASSUNG

Zwei Typen von Skelettveränderungen in Verbindung mit chronischer renaler Insuffizienz, wobei jeder Typ eine verschiedene Pathogenese zu haben scheint, werden beschrieben und besprochen. Ein gelegentliches Vorhandensein von Knochenveränderungen auf Thorax- oder gewöhnlichen Abdomenröntgenbildern bei Fällen von chronischer renaler Insuffizienz ist auf renale Osteodystrophie verdächtig.

RÉSUMÉ

L'auteur décrit et analyse deux types de lésions squelettiques liées à l'insuffisance rénale chronique, chaque type de lésion semblant avoir une pathogénie différente. La constatation fortuite de lésions osseuses sur des radiographies du thorax ou de l'abdomen dans des cas d'insuffisance rénale chronique doit faire penser à une ostéodystrophie rénale.

REFERENCES

ALBRIGHT, F., DRAKE, T. and SULKOWITCH, H. W.: Renal osteitis fibrosa cystica. Report of a case with discussion of metabolic aspects. Bull. Johns Hopk. Hosp. 60 (1937) 377.

— BAIRD, P. C., COPE, O. and BLOOMBERG, E.: Study on the physiology of the parathyroid glands IV. Amer. J. med. Sci. 187 (1934) 49.

ANDERSEN, D. H. and SCHLESINGER, E. R.: Renal hyperparathyroidism with calcification of the arteries in infancy. Amer. J. Dis. Child 63 (1942) 102.

BAKER, S. L.: General softening of bone due to metabolic causes. Brit. J. Radiol. 27 (1954) 609.

BARBER, H.: Renal dwarfism. Quart. J. Med. 14 (1920—21) 205.

BERGSTRAND, H.: Parathyreoideastudien II. Acta med. Scand. 54 (1921) 539.

BRAILSFORD, J. F.: Slipping of epiphysis of head of femur: its relation to renal rickets. Lancet 1933 I p. 16.

BROOKFIELD, R. W., RUBIN, F. I. and ALEXANDER, M. K.: Osteosclerosis in renal failure. Fac. Radiol. 7 (1955) 102.

CAMP, J. D. and OCHSNER, H. C.: Osseous changes in hyperparathyroidism associated with parathyroid tumor. Radiology 17 (1931) 63.

CANCELMO, J. J. and BROMER, R. S.: Osteonephropathy in children. Amer. J. Roentgenol. 65 (1951) 889.

CHOWN, B.: Renal rickets and dwarfism: a pituitary disease. Brit. J. Surg. 23 (1935—36) 552.

CRAWFORD, R., DENT, C. E., LUCAS, P. et coll.: Osteosclerosis associated with chronic renal failure. Lancet 1954 II p. 981.

DENT, C. E.: Rickets and osteomalacia from renal tubular defects. Bone Jt Surg. 34B (1952) 266.

— and HODSON, C. J.: Radiological changes associated with certain metabolic bone diseases. Brit. J. Radiol. 27 (1954) 605.

FLETCHER, H. M.: *Case of infantilism with polyuria and chronic renal disease. Proc. roy.* Soc. Med. 4 (1911) 95.

GILMOUR, J. R.: The parathyroid glands and skeleton in renal disease. Oxford University Press, London 1947.

GINZLER, A. M. and JAFFE, H. L.: Osseous findings in chronic renal insufficiency in adults. Amer. J. Path. 17 (1941) 293.

GLASGOW, J. F. and ROBINSON, A. W.: Subperiosteal bone resorption in hyperparathyroidism. *Brit. J. Radiol. 28 (1955) 381.*

GUTMAN A B and PARSONS W B Hyperparathyroidism simulating or associated with Paget's disease Amer Int Med 12 (1938) 13

HOLMAN C B Roentgen manifestations of vitamin D intoxication Radiology 59 1952 805

HUBBARD R S and WENTWORTH J A A case of metastatic calcification associated with chronic nephritis and hyperplasia of the parathyroids Proc Soc exp Biol 18 (1920—21) 307

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LEVIN R T and GENOVESE D C Report of a case of longstanding renal insufficiency with extensive metastatic calcifications (renal osteitis fibrosa Amer J Roentgenol 64 1950 473

LIGHTWOOD R A case of dwarfism and calcinosis associated with widespread arterial degeneration Arch Dis Childh 7 (1932) 193

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MITCHELL A G Nephrosclerosis in childhood with special reference to renal rickets Amer J Dis Child 40 (1930) 101 345

MULLIGAN R M Metastatic calcification Arch Path 43 (1947 I

NICHOLS B H and SHIFLETT E L Renal rickets with report of case Radiology 23 1934 67

PARSONS L G The bone changes occurring in renal and coeliac infantilism and their relationship to rickets Arch Dis Childh 2 (1927) 1

PENDERGRASS E P and BROOKS F I Report of a case of osteonephropathy with vascular calcification in infancy Radiology 62 (1954) 927

PUGH D G Subperiosteal resorption of bone Amer J Roentgenol 66 (1951 5 7

STANBURY S W Azotaemic renal osteodystrophy Brit Med Bull 13 (1957

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NON COLLAPSING AIR-FILLED ESOPHAGUS IN DISEASED AND POSTOPERATIVE CHESTS

by

GUNNAR BLOMQUIST and PAUL S MAHONEY

The esophagus is a self collapsing organ which normally does not contain air. If, however, the walls of the esophagus become fixed by scarring and adhesions to surrounding structures, its lumen may remain patent and fail to collapse: the esophagus will then contain air and be demonstrable on roentgen examination of the chest. It is imperative that the esophagus be correctly identified and differentiated from other air-containing structures within the chest.

A review of the literature has revealed a few references to the roentgen appearances of the esophagus in inflammatory diseases and postoperatively. HAWES (1944) described in detail the roentgenographic changes in the esophagus in tuberculous mediastinitis. He mentioned one case in which the esophagus failed to collapse secondarily to inflammatory changes within the mediastinum. He did not illustrate this abnormality nor did he emphasize its significance in the differential diagnosis. KORNBLUM & OSMOND (1934) described the classic changes found in non specific mediastinitis. They stressed the importance of an examination of the esophagus to complement the roentgen examination in all cases of mediastinitis. Deviation of a patent, rigid, barium filled esophagus in the mediastinum was illustrated by DE LORIMIER, MOEHRING & HANNAN (1956) in a case of apical tuberculosis following thoracoplasty

Submitted for publication 3 June 1960



a b

Fig 1 a) Air filled deviated esophagus Pleural margin of partially herniated right lung indicated by arrows b) Barium examination of the esophagus

These authors recognized that changes in the esophagus were the result of fixation of the esophageal walls to surrounding structures by scarring and adhesions but they did not recognize that this structure often appears as a linear air column in an ordinary roentgenogram and that its nature can be confirmed by a barium swallow

In recent years increasing progress has been made in thoracic surgery The frequency of the occurrence of an air filled esophagus secondary to mediastinitis has somewhat diminished as a result of early diagnosis and operation Chest surgery however involves resection not only of pulmonary tissue but often mediastinal tissue as well This fact in turn may result in non inflammatory scarring and adhesions of the walls of the esophagus which prevent the lumen from collapsing It is to this entity we wish to draw attention

Ten cases will be described of an air filled esophagus These cases have been selected to illustrate the major roentgenographic features as well as to demonstrate the importance of the appearances in the differential diagnosis of chest conditions



Fig 2 a) An air column partially overlaps the trachea b) Barium examination of the esophagus

Case reports

Case 1 Male aged 49 A large tumor surrounding and compressing the bronchus and displacing it towards the apical segment of the left lower lobe was found at thoracotomy Pneumonectomy was performed the visceral and mediastinal pleurae were found to be adherent and both layers had to be removed the aorta and the esophagus were exposed Roentgen examination four months later disclosed a linear air column with a sharp kink at the level of the carina extending beyond the confines of the mediastinum (Fig 1a) Examination of the esophagus with barium confirmed this structure to be the esophagus (Fig 1b)

Case 2 Male aged 42 complaining of wheezing on exhaling Tomography bronchography and bronchoscopy disclosed stenosis of the left main stem bronchus An unsuccessful attempt was made to resect the bronchus and affect an end to end anastomosis but in so doing a portion of the mediastinal pleura was stripped away Left pneumonectomy was performed Histology revealed chronic inflammatory tissue in the resected bronchus Seven months later

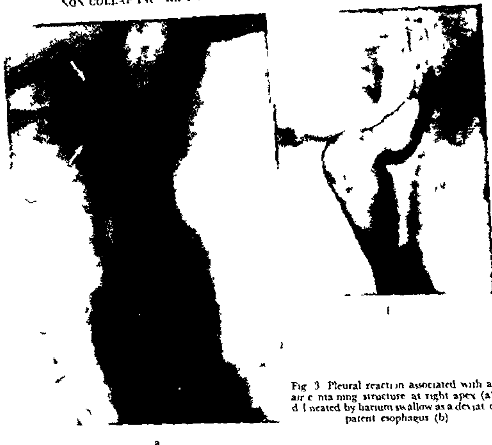


Fig 3 Pleural reaction associated with an air containing structure at right apex (a) delineated by barium swallow as a deviated patent esophagus (b)

roentgen examination of the chest demonstrated a linear air column extending from the thoracic inlet to the left cupola of the diaphragm and partially superimposed upon the tracheal air column and the pleural margin of the herniated right lung (Fig 2a) An examination of the esophagus with barium confirmed this structure to be the esophagus (Fig 2b)

Case 3 Male aged 62 underwent right middle and upper lobe lobectomy for adenocarcinoma A large flap of the posterior mediastinal pleura was freed to cover the exposed hilum but the esophagus was exposed Six weeks later roentgen examination disclosed right apical pleural reaction and an air filled cavity in this region (Fig 3a) A barium swallow examination showed that this structure was the esophagus (Fig 3b)

Case 4 Male aged 53 underwent left pneumonectomy for extensive bronchiectasis this being followed postoperatively by a left hemothorax this complication resolved spontaneously One month later the esophagus was shown roentgenographically to be air filled (Fig 4a) this was confirmed by a barium swallow (Fig 4b)

Case 5 Male aged 56 Left pneumothorax induced for pulmonary tuberculosis of left upper lobe Attacks of pleurisy then resulted in thickened pleura most marked in the left



Fig 4 a) Air in esophagus (↑) Border of herniated right lung (↑) Fluid level at left apex due to hemothorax b) A barium swallow shows the extent of the air filling of the esophagus and differentiates it from the tracheal air column and the herniated right lung

apical zone Roentgen examination of the chest one year later revealed displacement of the mediastinum as well as a linear gas column lateral to the trachea (Fig 5a) roentgen examination with barium showed this area to be part of the esophagus (Fig 5b)

Case 6 Male aged 42 developed pulmonary tuberculosis in the apical segment of the left lower lobe which spread to the right lung Recurrent attacks of pleurisy resulted in thickened pleura most marked on the left side Ten years later left lower lobe lobectomy and pulmonary decortication were performed Two months later a roentgen examination of the chest revealed three air containing structures at the left apex (Fig 6a) The two smaller round thin walled cavities overlapped one another and contained fluid levels the third structure consisted of a linear air column extending along the left border of the trachea and contained no fluid level A barium swallow showed the latter structure to be the esophagus (Fig 6b) The two other structures were loculated pleural effusions

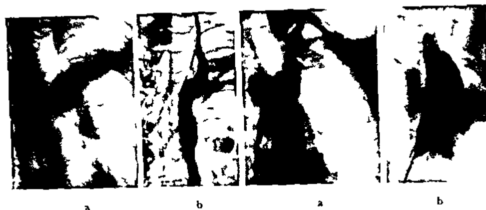


Fig 5 Linear air column just lateral to the deviated trachea at left apex (a) confirmed by barium swallow as being the esophagus (b)

Fig 6 Two overlapping air-containing structures with fluid levels at left apex Air filled esophagus lateral to the trachea contains no fluid level It is outlined with barium in (b)

Case 7 Male aged 38 contracted pulmonary tuberculosis of the apical segment of the left upper lobe thoracoplasty was performed Roentgen examination of the chest one year later revealed a linear air space lateral to the trachea which could have represented herniation of the apex of the left lung A barium swallow examination showed this structure to be the esophagus

Case 8 Female aged 60 developed pulmonary tuberculosis of the posterior apical segment of the right upper lobe (Fig 7 a and b) The lesion regressed slightly over a period of a year under medical care Bronchography was performed a year later During the procedure some contrast medium flowed into an air containing structure at the right apex This was at first incorrectly interpreted as a residual tuberculous cavity filled via the bronchus to the posterior

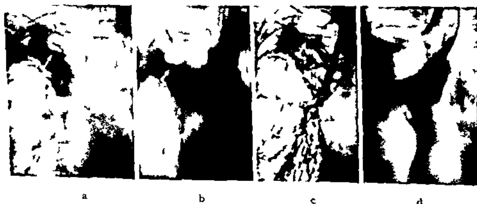


Fig 7 a) Rounded air filled structure just lateral to the deviated trachea at right apex b) Tomography separates the structure from the trachea by a distance equal to only the thickness of the tracheal wall Bronchography shows contrast medium outlining the structure d) Postoperative barium swallow examination disclosed the air structure to be a portion of a dilated air filled esophagus



Fig. 8. Linear air column to the right of trachea and extending obliquely across its lower end. b) The air distended esophagus is well outlined in the right lateral decubitus position.

apical segment (Fig. 7c), in fact it was a portion of the esophagus. At subsequent operation when the right upper lobe was resected, it was noted that the serous and muscular layers of the esophagus had split and allowed the mucosa to herniate into the right apex. The exposed esophageal mucosa had become fixed by adhesions to the surrounding inflammatory tissue in the lung and failed to collapse upon itself (Fig. 7d).

Case 9. Male, aged 74. This case was diagnosed as being one of tuberculosis of the right upper lobe and was followed periodically. Nine years later roentgen examination disclosed slight displacement of the mediastinum as well as a linear air column just to the right of the trachea (Fig. 8a). A barium swallow examination in both the upright and lateral decubitus positions correctly identified this structure as being the esophagus (Fig. 8b).

Case 10. Male, aged 59, developed sarcoidosis and was treated with cortisone. Two years later the patient was found to have a left pulmonary abscess which was treated conservatively; the cortisone was discontinued and the abscess resolved slowly. Three years later roentgen examination disclosed a residual cavity at the left apex and marked fibrosis at the left hilum with retraction of the mediastinum to the same side; a linear air structure was interpreted as air in the esophagus (Fig. 9a). A barium swallow examination confirmed the nature of the structure (Fig. 9b).

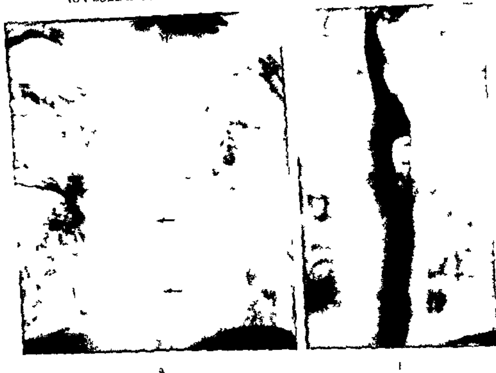


Fig 9 Extensive fibrosis in the lung field particularly on the left side with retraction of the mediastinum to that side Air filled esophagus outlined by *arrows* abscess cavity at left apex (b) A barium swallow examination shows that the air column represents the esophagus The lower part of the esophageal wall is thickened

Discussion

An air filled esophagus may sometimes be found in a roentgenographic examination of a diseased or postoperative chest The inflammatory reaction about the esophagus may be confined to the mediastinum but more often involves the lung pleura and mediastinum as well The esophagus will appear as a vertical linear air containing structure about 1 cm in diameter which is often curved kinked and deviated to one side of the chest Anatomically the esophagus is well anchored in its upper third, but is more freely mobile in its lower two thirds The esophagus will consequently be found to be only slightly deviated in the upper part of the chest and often situated just lateral to the trachea in the lower part of the chest, on the other hand the esophagus is usually markedly deviated to one side

Cases 1 and 2 are similar in that they both illustrate the typical appearance of the esophagus following an operative procedure within the thorax In Case 1 the esophagus was most displaced below the carina in which situation

its diameter was also widest. This portion of the esophagus lay in the region of the mediastinum where the surgeon had removed the mediastinal pleura and exposed the esophagus to postoperative scarring and adhesions, allowing it to become mobile and deviate to the left. In Cases 2 and 3 the dissection exposed the esophagus and rendered it prone to scarring and retraction in the subsequent postoperative healing phase.

In Case 4, the esophagus was deviated for two reasons: the scarring following the operative procedure and the resultant forces secondary to clot retraction initiated by a postoperative hemorrhage.

Cases 5, 6, and 7 illustrated the importance of a barium swallow examination to distinguish the esophagus from other air containing structures. The air column in Case 5 could have been misinterpreted as herniation of the apex of the right lung. In Case 6, the two thin walled air structures with fluid levels were by exclusion loculated pleural effusions. The third linear air column with no fluid level was, when filled with barium, shown to be the esophagus. The air column in Case 7 could readily have been mis diagnosed as herniation of the apex of the left lung. A roentgen examination with barium confirmed it to be the esophagus.

Case 8 was a peculiar one in which an air containing structure in the lung was incorrectly interpreted as a tuberculous cavity. The lesion actually represented a herniated part of the esophagus. During bronchography the patient inadvertently swallowed some of the contrast medium which subsequently filled the air structure and gave the impression that it was being filled via a bronchus.

Case 9 is included in the series to demonstrate the value of the lateral decubitus position to identify unknown air structures. In this case, the barium formed a pool in the structure and clearly identified it as the esophagus.

Case 10 demonstrates that two conditions occurring simultaneously within the thorax and both causing fibrosis and retraction, may complement one another in giving rise to air in the esophagus.

Anatomy and pathology. The anatomic position of the esophagus within the thorax renders the organ prone to involvement in any inflammatory reaction. Normally, the esophagus is a self collapsing organ, flattened in its antero posterior diameter and lying retrotracheally in front of and slightly to the left of the vertebral column. Its circumference is not of any great magnitude, but because the esophagus extends from the thoracic inlet to the diaphragm it presents a rather large surface area to a great number of anatomic structures. The esophagus is consequently prone to involvement in any pathologic process arising in adjacent structures.

This concept is particularly apparent with regard to the mediastinal pleura. GLADNIKOFF (1948) has demonstrated roentgenographically that structures once described as "mesenterium esophagei" are actually folds of mediastinal pleura

surrounding the esophagus These folds may be seen as thin linear densities lying between the barium filled esophagus and the air containing lung On the right side these pleural folds may be identified from the thoracic inlet to just above the right cupola of the diaphragm with a prominent bulge above the tracheal bifurcation corresponding to the arch of the azygos vein On the left side the pleura may be visible from the thoracic inlet to below the aortic arch These folds of pleura correspond to the anatomically described esophageal grooves in the right and left lungs respectively Any inflammatory process which involves the mediastinal pleura will therefore subsequently involve the serosal surface of the esophagus as well

Near the thoracic inlet the esophagus gives off numerous circular muscle fibers which are continuous with the inferior pharyngeal constrictor Accessory slips of muscle fibers tend to fix the esophagus in position between the left mediastinal pleura and the pericardium These supporting structures which are more numerous and effective in the upper third of the esophagus, tend to anchor its position within the thorax

Any process which tends to disrupt these supporting structures such as surgery or a dissecting mediastinal inflammatory process will free the esophagus and allow it to deviate to one side Since these supporting structures are poorly developed in the lower part of the esophagus the lower third will deviate more freely and to a greater extent than the upper third Similarly, any inflammatory process involving structures in direct contact with the esophagus such as the aortic arch the left main stem bronchus and the pericardium over the left atrium will in turn directly affect the esophagus

The walls of the esophagus may become rigid and fail to collapse in intrinsic conditions to which they are subject quite apart from any extrinsic process in the mediastinal pleura Scleroderma in which the walls are infiltrated with fibrous tissue may cause the esophagus to remain patent and similar esophageal changes with the same result may occur in conditions like scirrhous carcinoma and achalasia of the cardia

Differential diagnosis The air filled esophagus should be differentiated from air containing structures such as loculated effusions abscess cavities lung herniations and cysts There are three roentgen features which are of importance in identifying the esophagus (1) The often characteristic vertical linear and tortuous shape of the structure The air column is usually of uniform diameter (approximately 1 cm) and is located along the course of the esophagus at all levels (2) The absence of a fluid level (3) The delineation of the esophagus with barium

SUMMARY

An air filled esophagus is often found on roentgen examination of diseased and post operative chests and must be differentiated from other air-containing structures Ten cases to illustrate th s condition are presented and discussed

its diameter was also widest This portion of the esophagus lay in the region of the mediastinum where the surgeon had removed the mediastinal pleura and exposed the esophagus to postoperative scarring and adhesions, allowing it to become mobile and deviate to the left In Cases 2 and 3 the dissection exposed the esophagus and rendered it prone to scarring and retraction in the subsequent postoperative healing phase

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CORRELATION OF ROENTGEN ANATOMIC CHANGES AND FUNCTIONAL TESTS OF THE KIDNEYS IN HYPERPARATHYROIDISM

by

N P G EDLING C A FOVALL and C G HELANDER

In a previous paper (1960) the present authors reported on the relation of urography to inulin and PAH (para aminohippuric acid) clearance and concentration tests performed in a series of cases of hyperparathyroidism This paper reports a study on the relations of roentgen anatomic changes in the kidneys including size and the presence of calcifications to the functional tests in the same material

Material and Methods The present series comprises 29 cases of hyperparathyroidism in which the blood calcium initially elevated reverted to normal after parathyroidectomy Two of the patients were subjected to nephrectomy for concretions

Routine roentgenograms of the kidneys were taken before and after the operation in 28 cases and in one case only postoperatively In many cases control examinations were performed before and after operation As to the size of the kidneys in routine films a length of 10 to 15 cm and a width of 5 to 8 cm are regarded as normal

A total of 38 urographies in 18 of the patients are reported all performed

Submitted for publication 16 May 1960

ZUSAMMENFASSUNG

Ein luftgefullter Ösophagus wird oft bei Rontgenuntersuchung von Thoraxerkrankungen und im Anschluss an Thoraxoperationen gefunden und muss von anderen luftenthaltenden Strukturen unterschieden werden. Zehn Fälle, die solche Zustände illustrieren, werden beschrieben.

RÉSUMÉ

Les radiographies de thorax pathologiques ou operés montrent souvent un oesophage plein d'air qu'il faut distinguer d'autres structures contenant de l'air. Les auteurs présentent dix cas illustrant cet état.

REFERENCES

DE LORIMIER, A. A., MOEHRING, H. G., and HANNAN, J. R. Clinical roentgenology. Vol. 4. Charles C. Thomas, Springfield, 1956.

GLADNIKOFF, H. Roentgenographic study of the mediastinum in health and in primary pulmonary carcinoma. Acta radiol. (1948) Suppl. No. 73.

HAWES, L. E. The roentgenological changes in the esophagus in tuberculous mediastinitis. Amer. J. Roentgenol. 51 (1944), 575.

KORNBLUM, K., and OSMOND, L. A. Mediastinitis. Amer. J. Roentgenol. 32 (1934), 23.



Fig 1 Hyperparathyroid m left kidney Parathyroidectomy in January 1957 a) In August 1953 the length of the kidney was 14 cm and the width 7 5 cm Calcinosis b) In May 1959 the length of the kidney was 12 5 cm and the width 6 5 cm Reduction in the distribution of the calcifications

included) The calcifications were passed in 3 cases during the course of the follow up examinations but remained unaltered or changed slightly in number and size in the remaining 22 cases

The six patients in whom kidney size decreased included 5 of the 10 cases of calcinosis and one with a slight degree of unilateral lithiasis The clearance values were lowered in all 6 cases The concentration power also low pre operatively remained unchanged in 5 and improved without reaching normal limits in one case postoperatively The excretion on urography at 6 examinations performed in 3 of the cases showed density to be good in one and poor in 2 cases

In the remaining 5 cases of calcinosis the size of the kidneys did not change during the period of observation The clearance values were normal in one and lowered in 4 cases The concentration power was low in all cases pre operatively it remained unchanged in one and improved in 4 — in one of

with a contrast medium dose of 40 ml Urografin 60 % (sodium + methyl glucamine diatrizoate) They were performed both before and after operation in 6 cases, and only postoperatively in 12 cases The urographic density was estimated subjectively and termed either normal or poor The degree of the contrast density of the pelves was the same in control examinations in the individual patients

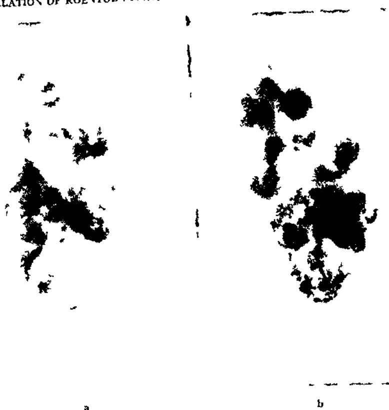
The analytic methods used for the clearance determinations have been described by EDVALL (1958) Bladder urine was used at all clearances except upon one occasion when selective examinations of the individual kidneys were done by ureteral catheterization Normal values in both kidneys for inulin clearance are 92 to 146 ml/min, and for PAH clearance 400 to 700 ml/min In the current series, inulin and PAH clearances were measured in 14 cases both before and after parathyroidectomy, in 5 cases only preoperatively, and in 10 cases only postoperatively, altogether 51 examinations were performed In the cases examined both before and after operation, initially normal clearance values remained at normal limits and reduced values persisted postoperatively except in three cases In these exceptions, either the inulin or PAH values were altered from normal to reduced or from reduced to normal postoperatively

According to HELLSTROM (1959), the concentration power of the kidneys in hyperparathyroidism is lowered but improves in most instances after parathyroidectomy Normal values are 1 025 and over The concentration power of the kidneys in the present series was examined in 28 cases both before and after operation, and in one case only postoperatively, the concentration tests were performed several times in many of the cases With the exception of one in which the value was at the lower limit of 1 025, the twenty eight cases displayed reduced values preoperatively

Results

The initial size of the kidneys in the present series before parathyroidectomy was as follows larger than normal unilaterally in 2 cases (single kidneys), smaller than normal unilaterally in one case (pyelonephritic shrinkage), and normal bilaterally in the remaining 25 cases When followed up during the course of the disease the size was found to be unchanged in 22 cases and decreased in both kidneys in 6 cases (Figs 1 and 2) The reduction in length was 1 to 2 cm and in width 0 5 to 1 cm In the remaining case, examined after operation only, one kidney was non excreting and of normal size while its fellow showed compensatory hypertrophy, both remained unchanged in size on follow up examinations Variations in size due to stasis are, of course, not included

Renal calcifications were present in 25 of the 29 cases Of these patients, 10 had bilateral nephrocalcinosis with or without lithiasis (Figs 1 and 2) and 15 had unilateral or bilateral multiple nephrolithiasis (the two single kidneys



a b

Fig 1 Hyperparathyroidism left kidney Parathyroidectomy in January 1957 a) In August 1953 the length of the kidney was 14 cm and the width 5 cm Calcinosis b) In May 1959 the length of the kidney was 12 5 cm and the width 6 5 cm Reduction in the distribution of the calcifications

included) The calcifications were passed in 3 cases during the course of the follow up *examinations* but remained unaltered or changed slightly in number and size in the remaining 22 cases

The six patients in *whom kidney size decreased* included 5 of the 10 cases of calcinosis and one with a slight degree of unilateral lithiasis The clearance values were *lowered in all* 6 cases The concentration power also low pre operatively *remained unchanged* in 5 and improved without reaching normal limits in one case postoperatively The excretion on urography at 6 examinations performed in 3 *of the cases* showed density to be good in one and poor in 2 cases

In the remaining 5 cases of calcinosis the size of the kidneys did not change during the period of observation The clearance values were normal in one and lowered in 4 cases The concentration power was low in all cases pre operatively, it remained unchanged in one and improved in 4 — in one of

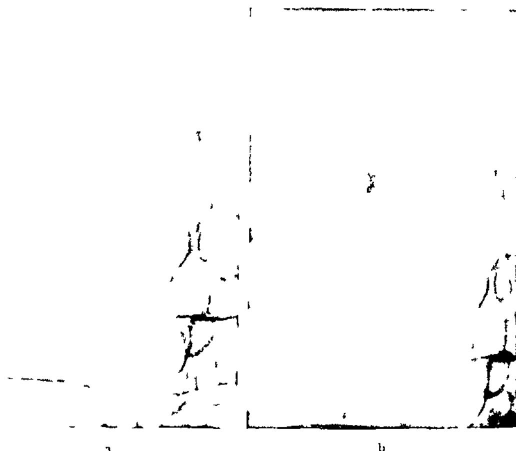


Fig 2 Hyperparathyroidism right kidney Parathyroidectomy in April 1954 a) In March 1954 the length of the kidney was 11 cm and the width just over 5 cm b) In May 1957 the length was 9 cm and the width just over 4 5 cm Slight calcinosis unchanged

them to normal limits — postoperatively Ten urographies performed in 4 of the cases showed density to be good in 3 and poor in one case

In the 10 cases of calcinosis, then, the size of the kidneys decreased in 5, the clearance values were low in all but one, and the concentration power improved in 5 cases, urography showed density to be good in 4 and poor in 3 of the 7 cases so examined

Of the 14 remaining patients with lithiasis, 5 had unilateral and 9 bilateral stones The kidneys remained unchanged in size during the period of examination The clearance values were normal in one of the cases with unilateral and in 5 of those with bilateral stones, in the remaining 8 cases the values were low However, in 3 of the latter 8 cases, only one of the clearance tests gave reduced values either pre or postoperatively With the exception of one case with unilateral stones, the concentration power improved in all 14 cases *examined* both pre and postoperatively, reverting to *normal in more than* half the cases

In the 4 patients without calcifications the kidney size remained unaltered The clearance values were normal in one and reduced in 3 cases The concentration power improved after parathyroidectomy in all 4 cases reverting to normal in two of them

Twenty four urographies performed in 9 of the patients with and 2 of those without lithiasis showed density to be good in 7 of the former and one of the latter, while it was poor in the 3 remaining cases

Discussion

The kidneys are known to be affected adversely during the course of hyperparathyroidism The presence of calcifications and the disturbance in the concentration power is discussed by HELLSTRÖM (1959) among others and the disturbance in glomerular filtration and tubular excretion by EDVALL (1958) Closer study of the roentgen anatomy and function of the kidneys revealed further details

In some of the cases there was a decrease in the size of the kidneys suggesting shrinkage of the renal tissues The process seemed to be slow starting before the parathyroidectomy and continuing postoperatively These cases had a higher incidence of calcinosis and of reduced renal function than the kidneys which kept their size It follows that calcinosis of small kidneys in hyperparathyroidism is indicative of fairly severe renal damage

EDVALL (1958) noted that the most advanced renal damage in hyperparathyroidism was found in patients with dysfibroplasia whether or not they had calcifications in the kidneys However, renal function was normal in only one of the cases of calcinosis in the present series and in half of them the kidneys decreased in size On the other hand there was in the main no obvious difference as regards functional capacity between kidneys with and those without lithiasis

Urography showed the density of the pelves to be good in some of the cases, despite the reduction in renal capacity According to EDLING & coll (1960) this is attributable to the damage to renal capacity in these cases not being more severe than can be compensated by technical measures such as dehydration of the patient and ureteral compression Density was poor in a larger proportion of the cases of calcinosis than of those with or without lithiasis

The incidence of kidneys with multiple calcifications in the series is very high When present in a routine film renal calcifications therefore indicate testing of the blood calcium level

SUMMARY

The relations between the size of the kidneys and the presence of calcifications on the one hand and the inulin and PAH clearance the concentration test and urography on the other were studied in 29 cases of hyperparathyroidism A decrease in the size of the kidneys and the presence of calcinosis are usually indicative of reduced renal capacity

ZUSAMMENFASSUNG

Die Beziehungen zwischen der Grosse der Nieren und dem Vorkommen von Verkalkungen einerseits und dem Inulin und PAH clearance, dem Konzentrationsversuch und der Urographie andererseits wurden an 29 Fällen von Hyperparathyreoidismus studiert. Eine Abnahme der Nierengrosse und ein Vorhandensein von Kalzinose sind als Zeichen einer herabgesetzten Nierenfunktion anzusehen.

RÉSUMÉ

Les auteurs ont étudié dans 29 cas d'hyperparathyroïdie les relations entre les dimensions des reins et la présence de calcifications d'une part, et les clearances à l'inuline et au PAH, l'épreuve de concentration et l'urographie d'autre part. La diminution des dimensions des reins et la présence de calcinose indiquent habituellement une diminution de la valeur fonctionelle des reins.

REFERENCES

EDLING, N. P. C., EDVALL, C. A. and HELANDER, C. C.: Correlation of urography and tests of renal function. Acta radiol. 54 (1960), 433.

EDVALL, C. A.: Renal function in hyperparathyroidism. Acta chir. scand. (1958) Suppl. No. 229.

HELLSTROM, J.: Primär hyperparathyroidism. (In Swedish.) Nordisk Med. 61 (1959), 551.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR O SANDSTROM)
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ROENTGENOLOGIC DETERMINATION OF THE LIVER VOLUME

by

L WALK

Although the liver may be identified in the conventional roentgenogram and methods to improve the visibility by means of pneumoperitoneum contrast media or inflation of the stomach or colon with gas have been described no adequate means of determining the size of the liver is to be found in the literature Roentgenologic studies of the size (ref 3 to 7, 10 to 14 16 19 to 21) or the volume (4 10 18) of the liver have included no autopsy controls except a report of a *liver index* (20) which showed a considerable error of calculation A method of *measurement* of the volume of the organ in experimental animals (1) is not adaptable for *clinical purpose*

The *size of the* liver estimated by clinical palpation differs considerably from that found at autopsy (19) *moreover* the palpability varies from case to case and is difficult to *evaluate* (9 15 17) A roentgenologic method of determination of the liver volume which is *now described* provides an accurate means of mensuration and is a valuable clinical *adjunct*

Material and Method

Roentgenograms of the liver were made immediately before opening the abdomen and the roentgenologic *measurements* of the organ were compared to the postmortem specimen in a material of 80 autopsies

Submitted for publication 11 July 1960

ZUSAMMENFASSUNG

Die Beziehungen zwischen der Grosse der Nieren und dem Vorkommen von Verkalkungen einerseits und dem Inulin und PAH clearance dem Konzentrationsversuch und der Urographie andererseits wurden an 29 Fallen von Hyperparathyreoidismus studiert Eine Abnahme der Nierengrosse und ein Vorhandensein von Kalzinose sind als Zeichen einer herabgesetzten Nierenfunktion anzusehen

RÉSUMÉ

Les auteurs ont étudié dans 29 cas d hyperparathyroidie les relations entre les dimensions des reins et la présence de calcifications d une part et les clearances à l inuline et au PAH l épreuve de concentration et l urographie d autre part La diminution des dimensions des reins et la présence de calcinose indiquent habituellement une diminution de la valeur fonctionelle des reins

REFERENCES

EDLING N P G EDVALL C A and HELANDER C G Correlation of urography and tests of renal function Acta radiol 54 (1960) 433

EDVALL C A Renal function in hyperparathyroidism Acta chir scand (1958) Suppl No 229

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Fig 2 Roentgenologic measurement of liver for calculation of volume exposure I diameter A



Fig 3 Exposure II diameters B and C.

Fig 3

The right border of the liver is easily identified in conventional roentgenograms The lower surface is seen most distinctly where it abuts against the right kidney The upper surface is not to be distinguished from the diaphragm a fact which however causes only an insignificant error The left border of the liver is difficult or impossible to localize tomography does not much improve the visibility and special methods of identification (2 7) would make the measurement too complicated to be used in current work The left border was therefore considered to lie in the plane of the middle of the left cupola of the diaphragm As shown later this is a satisfactory approximation and considerably simplifies the measurement

Two roentgenograms are obtained at as great a focus film distance as possible (150 cm in autopsy cases and 120 cm in clinical cases) to reduce the error of projection Film size 30 × 40 cm

Exposure I The subject lies supine with the tube vertically above the liver area and the film horizontal (Fig 2) The distances of the focus to the film and to the middle of the patient s body are measured so that correction of the diameters in the roentgenograms to their actual size may be made

Exposure II The subject is rotated 50 to 60 degrees to the right the film now being placed vertically (Fig 3)

These positionings were employed in 51 autopsy cases but are also adequate for clinical use The following further positionings have been tested in 29 autopsy cases Exposure I^b as I but with the tube angled 20 degrees toward the head and Exposure II^b, as II but the tube angled 20 degrees toward the feet

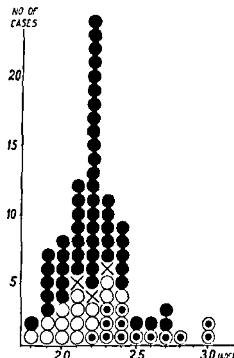


Fig 1 Index for calculation of liver volume from linear dimensions of autopsy specimen Analysis of 83 cases

(●) Normal configuration of liver
(○) Thin borders
(⊙) Blunt thick borders
(×) Riedel's lobe

In order that the volume of the liver could be calculated from the linear size, the lateral (A), a p (B) and vertical diameters (C) of the liver specimen were recorded and the volume determined by immersion of the specimen in a basin of water and measurement of the overflow The following formula was used

$$\frac{A \times B \times C}{\text{Index}} = \text{Liver volume}$$

The diameters and the volume of the specimen being known, the index may be determined for any case (Fig 1) The index, in a normal configuration of the liver, varies from 1 8 to 2 7 (average 2 25) Livers with a thin and flat left and/or right border have a greater index of 2 2 to 3 0 (average 2 6), whereas livers with blunt thick borders have a smaller index of 1 8 to 2 4 (average 2 1) Livers with a Riedel's lobe have a normal index

The volume of the specimen can thus be calculated with a maximal error of ± 20 per cent if consideration is given to the form of the organ

Roentgenologic mensuration

Because of the irregular oblique position of the liver in the abdomen, roentgenologic measurements cannot be directly compared to autopsy findings A technique of measurement, minimizing the error caused by the oblique position of the organ, had to be found



Fig 5 Thin right border of liver



Fig 6 Blunt rounded right border of liver

The error of calculation in the great majority of our cases does not exceed ± 16 per cent In a case of anomaly the error was 27 per cent the actual volume being smaller than calculated

Technique II (exposures I^b *and* II^b *diameters* A^b, B^b *and* C^b) The index has been determined in 29 autopsy cases (Fig 4) as 3 0 to 4 5 (average 3 75) for the normal liver 3 6 to 4 5 (average 4 05) with a thin right border of the organ and 3 0 to 4 0 (average 3 5) with a blunt thick border The error has been ± 20 per cent being less regularly distributed than in technique I

The question has been considered as to whether the diameter A might be more exact if the left lobe of the liver could be identified in the roentgenogram The position of the left border was recorded at autopsy and marked on the film (exposure I^b) the error of measurement was ± 17 per cent when compared with the autopsy diameter whereas by measurement from the middle of the left cupola of the diaphragm it was ± 15 per cent Identification of the left border of the liver would thus not improve the results moreover the method would become too complicated to be used in practice and would include an uncontrollable source of error

The precision of the volume calculation can probably be increased by use of diameter A^b (exposure I^b) B^b (exposure II^b) and C (exposure II) In these three projections any of the roentgenologic diameters has the smallest deviation from the autopsy diameter

Application

The great variability of the liver on palpation in healthy adults has been pointed out in the literature (15) it may be palpable from 700 grams as weighed at autopsy although a non palpable liver may be found to weigh up to 2 800 grams (19) In our material the liver has been palpable and described as 1 to 3 fingerbreadths from 1 200 ml displacement volume and 4 finger

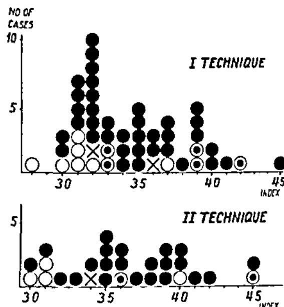


Fig. 4. Index for roentgenologic calculation of liver volume in an analysis of 51 autopsy cases examined by technique I and of 29 cases examined by technique II.

(●) Normal configuration of liver
(_) Thin right border
( ) Blunt rounded right border
( ) Riedel's lobe

Three diameters have been measured in the roentgenogram and corrected to their actual size: diameter A (exposure I), from the right border of the liver to the middle of the left cupola of the diaphragm; diameter B (exposure II), from the anterior border of the liver to the most distal part of its posterior surface as outlined by the diaphragm; diameter C (exposure II), from the lower surface of the liver, where it lies close to the upper pole of the kidney, in a transverse direction through the body of the liver to its upper surface at the lateral part of the diaphragm.

The liver volume has been calculated by the same formula as used for the autopsy material, but the index is different. Two techniques have been tried.

Technique I (exposures I and II, diameters A, B and C). The index has been determined in 51 autopsy cases (Fig. 4). The index, in a normal liver configuration, varies from 3.0 to 4.1 (average 3.55); with a thin flat right border of the liver, as seen in the roentgenogram (Fig. 5), it is 3.3 to 4.2 (average 3.75), whereas with a blunt thick border (Fig. 6) it is 2.8 to 3.7 (average 3.25). The index in one case was 4.5; the right lobe was pendulant but no characteristic thin border was seen in the film and the autopsy specimen revealed an anomaly of the left lobe which was narrow with an unusually small anteroposterior diameter.

These average sizes of the index, for any type of liver configuration, have been employed as follows:

1	Normal	3.55
2	Thin flat border	3.75 (in marked cases 4.0)
3	Blunt thick border	3.25

diastase value was found in 2 of the 3 cases with the greatest volume In cases previously operated on for biliary disease, and examined for cholangitis or for stones in the bile duct the volume was from 615 to 1 010 ml In diabetics the volume was frequently increased varying from 680 to 1 050 ml in pure cases and 1 270 to 1 360 ml in 3 cases complicated by cardiosclerosis cholangitis after cholecystectomy and adipose degeneration of the liver (verified by biopsy), respectively An increased volume was found in insulin treated alcoholics The relative volume in hepatitis varied from 960 to 1 600 ml in the course of the disease In cirrhosis it varied from 550 to 1 530 ml The relative volume was up to 1 270 ml in myeloid leukemia and up to 1 070 ml in lymphatic leukemia in polycythemia there was no marked increase of the volume In cardiac insufficiency the relative volume was calculated as being from 810 to 1 180 ml A marked increase in the volume is found in chronic pyelonephritis but normal values in chronic nephritis A slight increase in volume is, for example found in various other diseases and intoxications

Follow up examinations on 2 or 3 occasions were performed in 13 cases The relative volume 2 weeks after cholecystectomy was 50 to 70 ml greater than before the pre and postoperative determinations in 3 cases were 720 and 770 ml 880 and 935 ml and 660 and 730 ml respectively The postoperative course in these cases was normal In one case, with a probable subphrenic abscess following cholecystectomy, the relative volume after the operation was 185 ml greater than before (700 and 885 ml) the signs subsided after treatment with antibiotics As the calculated liver volume will include subphrenic fluid if present any marked increase in the volume after cholecystectomy may be of clinical significance In one case in which cholecystectomy had been previously performed the relative volume after removal of a stone from the bile duct was reduced by 110 ml (from 690 to 580) In a case of sprue in which a jejunocolic anastomosis had been performed because of terminal ileitis the volume diminished from 1 400 to 1 180 ml during a year of medical treatment Successive changes in the volume were also recorded in the remaining 7 follow up cases including a progressive increase from 810 to 860 and 890 ml in 18 months in a case of myelosclerosis

SUMMARY

A method of roentgenologic determination of the liver volume suitable for clinical use is described The error of the method is in the great majority of the cases less than ± 16 per cent In occasional cases it may be 27 per cent the actual volume being smaller than calculated

ZUSAMMENFASSUNG

Eine Methode der röntgenologischen Volumbestimmung der Leber für die klinische Arbeit geeignet wird beschrieben In der überwiegenden Mehrzahl der Fälle ist der Fehler der Methode höchstens ± 16 prozent In einzelnen Fällen kann er 27 Prozent betragen indem das Volumen kleiner ist als berechnet

Table

Clinical palpation of the liver compared to the relative volume (volume of autopsy specimen of liver per square meter of body surface) in an analysis of 50 autopsy cases

Liver on palpation	Relative liver volume				
	500—699 ml	700—899 ml	900—1 099 ml	1 100—1 499 ml	1 500 or more
Not palpable or palpable at costal margin	4	7	14	2	—
1 fingerbreadth	—	3	1	1	—
2 to 3 fingerbreadths	3	2	6	2	—
4 fingerbreadths or more	—	2	1	1	1

breadths' from 1 000 ml displacement volume. On the other hand, a non-palpable liver has been found to have a displacement volume of 2 500 ml at autopsy. This confirms that the evaluation of the liver by clinical palpation is difficult. The liver volume per square meter of the patient's body surface (relative volume of the liver) is more informative than the actual volume of the organ, and when compared to clinical palpation even the relative volume reveals the inadequacy of the palpation (see Table).

The relative volume has been determined in 304 cases by means of our technique I. It has varied from 520 to 1 850 ml.

Example of calculation. Diameter A is 31.5 cm, B 21.8 cm and C 13.2 cm in the film. The distance of the tube to the film is 120 cm and to the middle of the patient's body 102 cm. The corrected diameter A is 31.5 : 120 × 102 = = 26.8 cm, B 18.5 cm, and C 11.2 cm. The liver has a rounded blunt right border, and the index 3.25 is chosen for calculation of the volume which is thus 26.8 × 18.5 × 11.2 : 3.25 = 1 710 ml. The patient's height is 175 cm and weight 63.5 kg, from the diagram of Du Bois (Arch. Int. Med. 17 (1916), 863) the body surface is found to be 1.78 square meters. The relative volume is 1 710 : 1.78 = 960 ml (slightly increased).

The relative volume has varied from 550 to 860 ml in normal cases; a relative volume of 800 to 900 ml has been considered to be a borderline case, and when more than 900 ml to be enlarged.

In symptomless cholelithiasis the relative volume has been found to be normal, 575 to 850 ml, whereas in gallstones with colic and icterus it varied from 610 to 1 030 ml. In acute cholecystitis, it was as high as 960 ml, in 2 cases with a volume of 940 and 960 ml respectively, high diastase values indicated the presence of acute pancreatitis. In acute recurrent cholecystitis, the volume was up to 1 090 ml, greater than in ordinary cholecystitis, even here, a high

diastase value was found in 2 of the 3 cases with the greatest volume In cases previously operated on for biliary disease, and examined for cholangitis or for stones in the bile duct, the volume was from 615 to 1 010 ml In diabetics the volume was frequently increased varying from 680 to 1 050 ml in pure cases and 1 270 to 1 360 ml in 3 cases complicated by cardiosclerosis, cholangitis after cholecystectomy and adipose degeneration of the liver (verified by biopsy) respectively An increased volume was found in insulin treated alcoholics The relative volume in hepatitis varied from 960 to 1 600 ml in the course of the disease In cirrhosis it varied from 550 to 1 530 ml The relative volume was up to 1 270 ml in myeloid leukemia and up to 1 070 ml in lymphatic leukemia in polycythemia, there was no marked increase of the volume In cardiac insufficiency the relative volume was calculated as being from 810 to 1 180 ml A marked increase in the volume is found in chronic pyelonephritis but normal values in chronic nephritis A slight increase in volume is for example found in various other diseases and intoxications

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RÉSUMÉ

Description d'une méthode de détermination du volume du foie convenant pour des explorations cliniques. L'erreur de la méthode est dans la grande majorité des cas inférieure à ± 16 pour cent. Exceptionnellement elle peut atteindre 27 pour cent, le volume reel du foie étant inférieur au volume calculé.

REFERENCES

1 ADAMS-RAY, J., HAGBERG, S., HJELMSTROM, P. and OLSSON, S. I.: A roentgen stereophotogrammetric method for measurement of variations in the volume of organs in living animals. Angiology 5 (1954) 59.
2 BÉTOULIÈRES, P., CARABALONA, P., PELISSIER, M. et CANDON, J.: La pneumostratigraphie dans l'exploration du lobe gauche du foie. J. belge radiol. 39 (1956) 453.
3 FELDMAN, M.: Liver measurement. A comparative study on the relation of chronic gall bladder disease to the size of the liver. Radiology 10 (1928) 496.
4 FIORIOLI, W.: Die klinische Auswertung des röntgenologischen Lebermessverfahrens. Med. Klin. 48 (1953) 1138.
5 FLEISCHNER, F. C. and SAYEGH, V.: Assessment of the size of the liver. New Engl. J. Med. 259 (1958) 271.
6 KOHLER, A.: Totalröntgenogramme der Leber. Fortschr. Röntgenstr. 13 (1908) 145.
7 LACARENNE, P.: Délimitation et mensuration radiologique du foie et de la rate grace à l'insufflation rectale du gros intestin. Thèse. Dijon 1920.
8 LAFFEYRE, N. C., BÉTOULIÈRES, P., CARABALONA, P. et coll.: L'étude radiologique du lobe gauche du foie. Intérêt de la pneumostratigraphie abdominale. J. Radiol. Electrol. 35 (1954) 478.
9 LICHTMANN, S. S.: Diseases of the liver, gallbladder and bile ducts. Lea & Febiger, Philadelphia 1949.
10 LUTZ, P.: Zur Technik der röntgenologischen Lebergrossenbestimmung. Med. Klin. 48 (1953) 1137.
11 MARTIN, C. L.: Roentgenologic studies of the liver and spleen. Amer. J. Roentgenol. 37 (1937) 633.
12 MOHR, W.: Röntgenologische Erfassung der Milz- und Lebergrosse bei Malaria. Fortschr. Röntgenstr. 72 (1949) 93.
13 NIMPFI, W.: A new method for the determination of the size of the liver and spleen. Amer. J. Gastroent. 23 (1955) 147.
14 OSGOOD, C. W. and HABBE, J. E.: A clinical and roentgenologic study of factors influencing the palpability of the liver. Radiology 21 (1933) 66.
15 PALMER, E. D.: Palpability of the liver edge in healthy adults. U. S. armed Forces med. J. 9 (1958) 1685.
16 PFAHLER, G. E.: The measurement of the liver by means of roentgen rays based upon a study of 502 subjects. Amer. J. Roentgenol. 16 (1926) 558.
17 SCHIFF, L.: Cited by FLEISCHNER and SAYEGH.
18 TESCHENDORF, W.: Lehrbuch der röntgenologischen Differentialdiagnose der Bauchorgane. Georg Thieme, Stuttgart 1954.
19 ZELMAN, S.: Liver and spleen visualization by a simple roentgen contrast method. Ann. Int. Med. 34 (1951) 466.
20 — Necropsy evaluation of the gas contrast roentgen visualization of liver and spleen. Amer. J. med. Sci. 236 (1958) 747.
21 — and PICARD, C. M.: Roentgen and autopsy evaluation of percussion of the liver and spleen. Gastroenterology 29 (1955) 1037.

LABORATOIRE DE DOSIMETRIE DU SERVICE CENTRAL DE PROTECTION CONTRE LES RAYONNEMENTS IONISANTS (DIRECTEUR PROF L BUGNARD), DE L INSTITUT NATIONAL D HYGIENE PARIS, FRANCE

CONTRIBUTION A LA MESURE DES RAYONS ROENTGEN DANS LE DOMAINE DE 5 A 50 KV

par

A Allisy et Mlle A M Roux

L installation generale comprend une source de tension stabilisee un dispositif de mesure de la tension et du courant dans le tube a rayons roentgen ainsi qu un électrometre destine a la mesure des courants d ionisation

Generateur et appareils de mesure Le tube a rayons roentgen du type Machlett AEG 50 A possede une fenetre de béryllium d environ 1 mm d epaisseur et une anti cathode de tungstene Le courant maximal admissible dans ce tube est de 20 mA la tension maximale de 50 kV Le generateur haute tension analogue au modele Massiot K 2 N a ete modifie de maniere a ne fournir qu une tension negative par rapport a la masse l anti cathode du tube a rayons roentgen se trouvant obligatoirement a ce potentiel Apres modification le generateur fonctionne en redresseur a une alternance Nous y avons adjoint un condensateur d une capacite de 0 1 μ Farad situe dans la cuve du voltmetre haute tension

Une machine tournante suivie d un stabilisateur magnetique a commande electronique alimente l ensemble de l installation Le chauffage du tube a rayons roentgen est pourvu d une stabilisation supplementaire formee d un amplificateur qui voit à son entree un signal proportionnel au courant anodique du tube a rayons roentgen et dont la sortie constitue une impedance variable disposee en serie avec le filament du tube Il est necessaire de disposer à l entree de cet amplificateur un filtre passe bas pour eviter des oscillations

Soumis a la Rédaction 30 Mai 1960

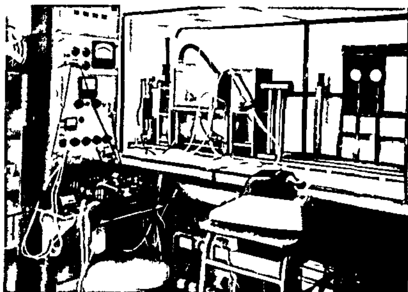


Fig. 1. Vue d'ensemble de l'installation de mesure des rayons roentgen très mous.

La haute tension est déterminée en mesurant le courant dans une résistance de 50 mégohms, ce courant atteint 1 milliampère sous une tension de 50 kV. La résistance globale est formée de 250 résistances de 200 kilo ohms. Chacune de ces résistances est connue à 0,5 ‰ près et peut dissiper une puissance de 2 watts. Le courant dans la chaîne de résistances ainsi que le courant dans le tube à rayons roentgen sont mesurés par une méthode d'opposition. La tension développée par ces courants aux bornes de résistances bobinées de haute précision est opposée à la force électromotrice d'un élément Weston. La sensibilité de cet appareillage de mesure a été déterminée pour contrôler la stabilité d'un point de fonctionnement plus que pour déterminer la valeur absolue des grandeurs à mesurer. Lors de la détermination des tensions, le galvanomètre dévie de 3 divisions pour une variation de 1 ‰ d'une tension de 5 kV et de 20 divisions pour une variation de 1 ‰ d'une tension de 50 kV. En mesurant le courant anodique du tube à rayons roentgen le galvanomètre dévie de 15 divisions pour une variation de 1 ‰ d'un courant de 5 mA. Les appareils de mesure qui viennent d'être décrits ainsi que la stabilisation du chauffage du tube à rayons roentgen sont disposés en dessous du banc de mesure (voir Fig. 1).

Mesure du courant d'ionisation. L'appareillage décrit est principalement utilisé à des fins de recherches sur les étalons, aussi les mesures sont elles effectuées à l'aide de deux chambres d'ionisation : la chambre à étudier d'une part, une chambre de comparaison ou pilote d'autre part. Nous utilisons un système électrométrique décrit ailleurs (1) formé d'une lampe électromètre pentode et d'un galvanomètre monté en opposition dans l'anode de la lampe. Le système

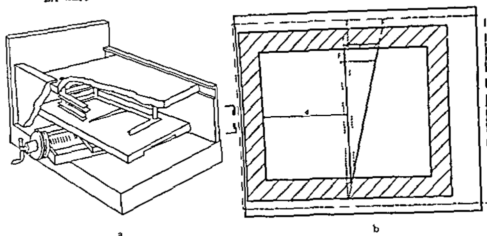


Fig 2 Schéma perspectif (a) et vue de dessus (b) de la chambre d'ionisation à parois d'air

a ete rendu symetrique en utilisant deux électrometres alimentes par la meme source de haute tension hautement stabilisee La source de tension variable ΔV destinee a la compensation de la charge des deux condensateurs de mesure, provient d un potentiometre de precision préalablement tare a l aide d un element Weston Cette tension ΔV est mise directement en serie avec le condensateur chargé par le courant d ionisation du pilote et par l intermediaire d un diviseur de potentiel de precision en serie avec le condensateur de mesure de la chambre etalon Ce diviseur de potentiel qui travaille a impedance d entree constante permet d afficher tous les rapports r, de 0 a 1 par bonds de 1/10 000 Le but de la mesure est alors de determiner r de maniere a compenser automatiquement la charge due au courant dans l etalon lorsque l on compense celle due au courant dans le pilote La compensation de la charge due au pilote peut etre manuelle ou electronique Une reproductibilite de $\pm$ 0 5‰ est aisement obtenue avec ce dispositif Les divers appareils de mesure ainsi que les alimentations stabilisees sont groupes sur un rack disposé a gauche sur Fig 1

Chambre d ionisation pilote Au cours de ce travail nous avons trouve que la chambre pilote la plus adequate etait formée par une deuxieme chambre a parois d air La construction de cette chambre peut etre beaucoup plus rudimentaire que celle de la chambre etalon mais il est important qu il y ait l epaisseur d attenuateur minimale entre les plaques de mesure des deux chambres (6) Chaque fois que l expérience le permet le pilote est dispose derriere l etalon (Fig 1) le faisceau traversant les deux chambres est ainsi délimité par le meme diaphragme Cette geometrie peut difficilement etre utilisee dans

la mesure des coefficients d'atténuation de l'air, dans ce cas, nous avons disposé une petite chambre pilote au voisinage de la fenêtre de béryllium du tube à rayons roentgen.

Lorsque le pilote est disposé derrière la chambre étalon, l'épaisseur d'air entre les deux plaques de mesure est de l'ordre de 30 cm. Cette couche d'air représente, à 10 kV, une atténuation de l'ordre de 60 %. La variation de cette atténuation est de 3‰ par degré centigrade, aussi avons-nous été conduits à disposer le tube à rayons roentgen, le banc de mesure et les chambres d'ionisation dans une enceinte réalisée en polystyrène expansé de 5 cm d'épaisseur, à l'intérieur de laquelle la température est maintenue constante. Cette enceinte est visible sur Fig. 1.

I. Description de la chambre d'étude à parois d'air

Une vue perspective schématique de la chambre à plaques parallèles est donnée en Fig. 2a et une vue de dessus de cette chambre en Fig. 2b, on y a porté les positions extrêmes (représentées par des traits pointillés), et médiane (représentée en traits pleins), du système plaque de mesure-plaques de garde (Fig. 2b). L'ensemble plaques de garde-plaque de mesure forme un rectangle de dimensions 30 cm × 25 cm. Les droites Γ_1, Γ''_1, Γ'_1 et Γ_2 passent par les milieux des fentes situées entre la plaque de mesure et les plaques de garde. Γ_1 et Γ_2 forment entre elles un angle d'environ 10 degrés, Γ_1 étant perpendiculaire au faisceau de rayons.

Le système plaque de mesure-plaques de garde peut subir une translation dans un plan horizontal parallèlement à la fente Γ_2 grâce à un dispositif porte-outil de tour qui est visible sur Fig. 2a. Les écarts de planéité de l'ensemble ne dépassent pas 1/100 millimètre. Le système de garde formé de cadres métalliques (zone hachurée Fig. 2b), est uniquement fixé à la plaque haute tension, l'ensemble pouvant être déplacé le long de l'axe du faisceau grâce à un système de glissières visibles sur Fig. 2a. La distance d (Fig. 2b) peut ainsi être modifiée. Les 6 cadres du système de garde ont des dimensions intérieures égales à 16 cm et 21 cm, leurs dimensions extérieures étant respectivement de 21 cm et 26 cm et leur épaisseur de 8/10 de mm ; ils sont distant entre eux de 8,6 mm à l'exception des cadres du milieu distants de 13,6 mm.

L'espacement entre plaque de mesure et plaque haute tension est de 7 cm, la longueur des plaques de garde de 13,5 cm ; la longueur moyenne de la plaque de mesure qui a la forme d'un trapèze rectangle est de l'ordre de 17 mm. Dans les deux positions extrêmes de mesure (Γ'_1 et Γ''_1, Fig. 2b) cette longueur est respectivement de 12 et 22 mm. Il est bien clair que la différence entre le courant d'ionisation correspondant à la longueur de 22 mm et celui correspondant à la longueur de 12 mm est équivalente à une mesure effectuée avec une plaque à bords parallèles ayant une longueur de $(10 - \varepsilon)$ mm, ε étant la largeur

de l'une des deux fentes supposées identiques Dans le cas de notre dispositif la largeur des fentes est éliminée lorsque l'on effectue une différence entre deux mesures a condition que les fentes soient rigoureusement parallèles Cette condition est facilement réalisable en pratique car les plaques de garde peuvent etre fixees sur le plan de référence en utilisant la plaque de mesure comme cale On réalise ainsi toutes les largeurs de fente désirables en deplaçant la cale plus ou moins le long d'un axe parallele a F_1 La plaque de mesure est posée sur trois plots d'ambre Un des plots vient placer son extremité conique dans un trou de la plaque l'autre qui se termine en forme de couteau s'engage dans une rainure et le troisieme hemispherique, est tangent à la plaque de mesure Ce support (point trait plan) permet de remettre toujours la plaque de mesure dans la meme position Il est commode, en particulier pour determiner l'influence du manque de planeité En remontant la plaque de mesure de 14/100 de mm par rapport aux plaques de garde nous avons mesure une variation de 2 % du courant d'ionisation moyen (correspondant a une longueur de mesure de 17 mm)

Soit l, la longueur de la plaque de mesure au niveau du faisceau pour une position donnee de la graduation du porte outil cette longueur n est, *en général* pas tres bien connue a cause d un reperage par rapport à l axe du faisceau qui est assez difficile Par contre la variation Δl pour un tour de la poignee du porte outil peut etre déterminee avec tres grande precision a l aide d un comparateur En relevant le courant d ionisation I en fonction du nombre de tours, on obtient une droite dans la mesure ou l attenuation des photons primaires par l air du volume de mesure est lineaire Etant donne qu il existe une relation linéaire entre le nombre de tours et la longueur l l *équation* de cette droite peut s ecrire

$$I = pl + q \tag{1}$$

En general nous relevons experimentalement 5 *points espaces* l un de l autre d une valeur Δl de l ordre de 2 mm La connaissance de *ces 5 points* permet de trouver les constantes p et q a l aide de la methode des moindres carres *Les ecarts entre* les points experimentaux et la droite atteignent rarement 1,5 ‰ La quantite $p = dI/dl$ qui represente l ionisation par unité de longueur permet la determination *de la dose* d exposition en roentgens

La chambre d ionisation qui vient d etre decrite a ete conçue de maniere a pouvoir etre transformee *facilement* en chambre etalon L ensemble amovible forme par le chariot porte *outil* les plaques de garde et la plaque de mesure (voir Fig 2a) peut etre *remplacé par* un systeme de plaques de garde entourant une plaque de mesure de 15 *mm* de largeur a bords paralleles La possibilite de deplacement de la *plaque haute tension* et du dispositif de garde est conservee ce qui permet une *reduction importante* de la longueur d air située entre le diaphragme et la plaque de mesure

Tableau

Rayonnement	kV	mA	Filtration inhérent approximative	Filtration additionnelle mm Al	1ère CDA	2ème DCA	Facteur d'homogénéité	a × 10	b × 10
A	5	5	195 mm Air + 1 mm Be	—	91,5 mm Air	99 5 mm Air	0 92	—	—
B	10	5	195 mm Air + 1 mm Be	—	0 024 mm Al	0 031 mm Al	0 77	3 022	2 637
C	20	2	195 mm Air + 1 mm Be	—	0 041 mm Al	0 076 mm Al	0 67	1,578	0 1769
D	40	1	195 mm Air + 1 mm Be	—	0 066 mm Al	0 095 mm Al	0 70	1 158	0 114
E	30	2	195 mm Air + 1 mm Be	0 097	0 101 mm Al	0 141 mm Al	0 72	0 690	0 173
F	30	2	195 mm Air + 1 mm Be	0 202	0 144 mm Al	0 232 mm Al	0 62	0 519	0 0181
G	30	5	195 mm Air + 1 mm Be	0 502	0 349 mm Al	0 556 mm Al	0 63	0 258	— 0 0184
H	40	2	195 mm Air + 1 mm Be	0 599	0 550 mm Al	0 915 mm Al	0 60	0 1857	— 0 0364
I	40	2	195 mm Air + 1 mm Be	1 303	0 992 mm Al	1 328 mm Al	0 75	0 0972	— 0 00456

II. Conditions expérimentales

Le Tableau donné ci-dessus indique les diverses conditions expérimentales dans lesquelles les mesures ont été effectuées. Nous avons donné pour chaque rayonnement, *caractérisé par une lettre*, les *conditions électriques*, les filtrations inhérentes et additionnelles ainsi que les premières et deuxièmes CDA. En général, les CDA sont exprimées en mm d'aluminium, à l'exception du rayonnement émis sous 5 kV pour lequel les épaisseurs d'aluminium étaient trop faibles pour pouvoir être déterminées avec précision. Nous avons exprimé ces CDA en mm d'air (760 mm Hg, 20° C). Pour être plus explicite dans la caractérisation de la qualité d'un rayonnement, nous avons introduit le facteur d'homogénéité qui est le quotient de la première CDA par la seconde. Nous avons retrouvé (Fig. 3) les anomalies de ce facteur qui ont été mises en évidence et expliquées par Zieler (17, 18). En comparant nos valeurs de CDA en fonction de la filtration totale à celles de Zieler (18), nous avons remarqué qu'à filtration égale nos CDA étaient, en général, supérieures de l'ordre de 10 %. Cet écart peut s'expliquer par l'incertitude dans la détermination de l'équivalence béryllium-aluminium et air-aluminium ou par des différences de pureté de l'aluminium utilisé.

Une autre explication plausible de ces écarts peut être donnée par le fait que les composantes alternatives superposées à la haute tension semblent assez différentes dans les deux expériences.

Fig. 4 indique les valeurs de l'ondulation, r, en fonction de l'admittance de charge du générateur, r est défini (9) par

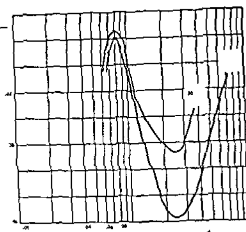


Fig 3 Variation du facteur d homogénéité en fonction de la CDA

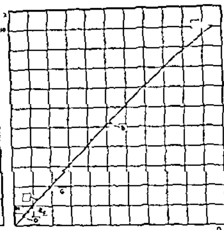


Fig 4 Variation du ronflement en fonction de l admittance de charge

$$r\,\% = 200\,\frac{V_M - V_m}{V_M + V_m}$$

ou V_M représente la valeur maximale et V_m la valeur minimale de la tension du generateur

Pour permettre la mesure de rayonnements tres mous sans avoir les inconvénients d un débit de dose d exposition trop important et d une geometrie incertaine, nous avons dispose entre la fenetre de beryllium du tube à rayons roentgen et le diaphragme de la chambre étalon un cylindre raccorde a une *pompe a vide primaire* (Fig 1) Ce cylindre est fermé par deux fenetres de terephtalate de polyethylene glycol (mylar) d une epaisseur de 0 84 *mg/cm²* *chacune* Ces fenetres etant sur le trajet du rayonnement il est intéressant de connaitre l equivalence air terephtalate en fonction de la qualité du rayonnement Entre 5 kV feu nu (rayonnement A Tableau) et 40 kV 1 3 *mm Al* (rayonnement I Tableau) nous avons trouve une equivalence constante a 3 % pres Nous admettrons dans ce domaine que 1 mg/cm² de terephtalate est equivalent a 0 71 mg/cm² d air

III Determination des facteurs de correction de la chambre d'ionisation a parois d'air

A Attenuation par l air

Il existe un grand nombre de publications concernant l attenuation de l air (3 4 10 12 13 18) mais les conditions experimentales sont souvent difficilement comparables Dans ce qui suit nous donnerons l attenuation de

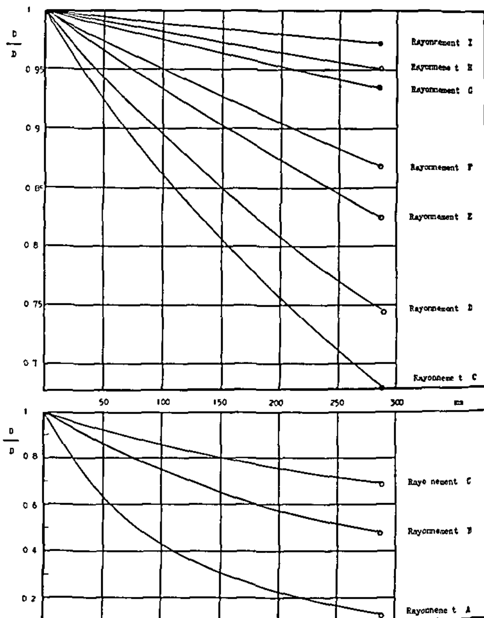
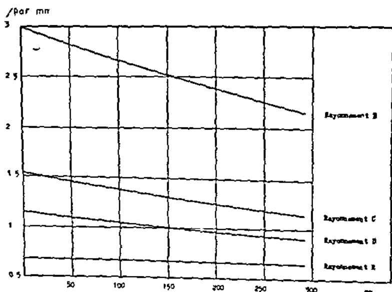


Fig 5 Attenuation de la dose d exposition par l air à 20 C et 760 mm Hg (Voir le Tableau p 62)

la dose d exposition par l air Les coefficients trouves sont utilisables pour le calcul des corrections dans la chambre etalon, il ne faut pas les confondre, comme JAEGER (5) l a montre avec les coefficients d'attenuation de l'energie determines, par exemple, a l'aide d une chambre à absorption totale (2) Figs 5 et 6 donnent nos resultats L air qui a servi a la mesure était sec et les valeurs ont ete normalisees a 20° C et 760 mm Hg Les rayonnements utilisés sont caracterises dans le Tableau, p 62 Pour mettre en évidence l absence



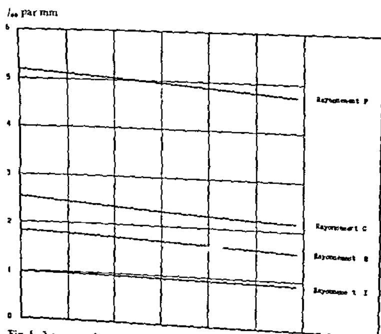


Fig 6 Variation de l'atténuation de la dose d'exposition par l'air (20 C et 760 mm Hg) en fonction de l'épaisseur d'air traversé (l'épaisseur nulle correspondant aux conditions du Tableau p 67)

d'erreurs dues a la géometrie ou a la diffusion, nous avons mesuré l'attenuation dans 290 mm d'air par deux méthodes differentes La premiere, utilisee pour le releve des courbes (Figs 5 et 6), consistant a déplacer la chambre étalon en laissant le diaphragme fixe Dans la seconde methode, nous avons remplacé le vide dans le cylindre par de l'air a la pression atmospherique (points experimentaux, Fig 5) Les deux methodes ont donne des resultats concordants a 1°/₀₀ pres Etant donne la précision des résultats, nous avons recherché un moyen pratique et precis permettant de calculer les corrections dues a l'attenuation de l'air Ceci est possible en remarquant que la fonction D_0/D ($D =$ = dose d'exposition) varie sensiblement linéairement entre $l = 0$ correspondant a D_0 et $l = 300$ mm d air sec a 20° C et 760 mm Hg Par la methode des moindres carrés, il est possible de mettre D_0/D sous la forme

$$\frac{D_0}{D} = al + bl^2 + 1 \quad (l \text{ etant exprime en mm})$$

Les coefficients a et b sont donnes dans le Tableau, p 62 Le desaccord entre les points experimentaux et la courbe ne depasse jamais 1°/₀₀

A partir de l equation

$$\frac{D_0}{D} = al + bl^2 + 1$$

il est facile de calculer la variation relative de l attenuation de la dose d'exposition

$$\frac{dD}{D\ dl} = \frac{a + 2\ bl}{1 + al + bl^2}$$

en fonction de l (Fig 6)

B Déformation du champ électrique

Les causes principales de deformation du champ électrique sont le manque de planeite entre la plaque de mesure et les plaques de garde, la presence du systeme de garde et les differences de potentiel de contact entre plaque de mesure et plaques de garde Les resultats concernant la premiere cause d'erreur ont ete donnés plus haut On se propose d examiner dans ce paragraphe les deux autres causes d erreur

1 *Déformation du champ électrique par le systeme de garde* Cet effet a été examine pour diverses positions du systeme de garde par rapport a la plaque de mesure

a) *Le systeme de garde est en position normale* (*Fig 2b*) Pour effectuer cette etude, on a dispose, autour du systeme de garde, un blindage de dimensions 31,4 cm × 23 cm (represente par une succession de traits longs et de traits courts sur la figure), susceptible d etre porte alternativement au potentiel de

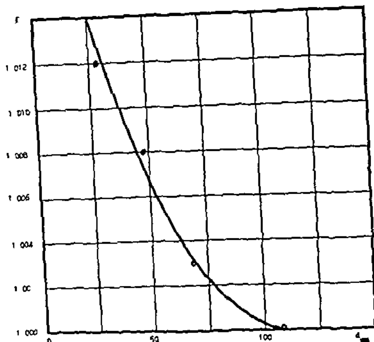


Fig 7 Deformation du champ électrique Facteur de correction en fonction de la distance entre systeme de garde et centre de la plaque de mesure (cf la figure 2b)

la masse ou a celui de la haute tension La construction de la chambre permettant de mettre en place ou de supprimer facilement le systeme de garde on a d abord determiné pour diverses longueurs de la plaque de mesure, les courants d ionisation I_0 et I_{HT} en l absence de systeme de garde le blindage etant relie successivement a la masse et à la haute tension Ces mesures revelent une augmentation de 7‰ des courants d ionisation lorsque le potentiel du blindage passe de la masse a la haute tension Les courants d ionisation I_g sont ensuite determines avec le systeme de garde en place On n observe alors aucun écart lorsque le blindage est relie a la masse ou a la haute tension Les valeurs de I_g se placent a mi chemin entre I_{HT} et I_0 à mieux que 0 5 ‰ pres

b) *Le systeme de garde est deplace par rapport a la plaque de mesure* Pour réduire l attenuation de l air le systeme de garde peut se deplacer le long de l axe du faisceau la plaque de mesure et les plaques de garde restant fixes Nous avons pu ainsi tester la déformation produite lorsque la distance d (Fig 2b) varie Les droites $I = pl + q$ ont été déterminées pour différentes positions du systeme de garde correspondant a des distances d variant de 108 a 28 mm Les valeurs de I et de p diminuent lorsque la distance d diminue

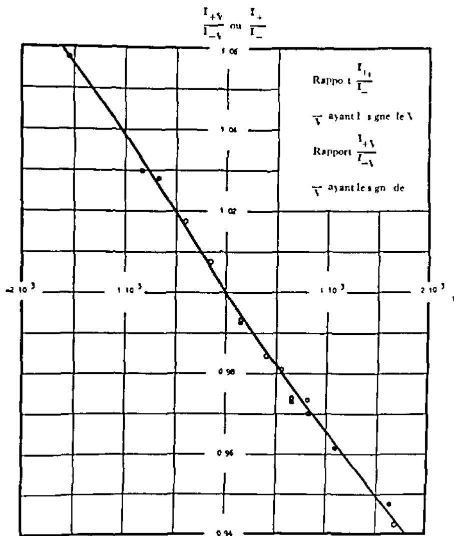


Fig. 8. Influence d'une différence de potentiel entre plaque de mesure et plaques de garde.

Nous avons tracé la courbe (Fig. 7) donnant le facteur de correction dans le cas d'une plaque parallèle de longueur $\Gamma_1\Gamma_1$ (Fig. 2b) en fonction de la distance d. Ce facteur est égal à 1 lorsque le système de garde se trouve en position normale, c'est-à-dire pour $d = 108$ mm. La courbe a été déterminée à 20 kV (rayonnement C-Tableau p. 62).

Dans cette expérience, la distance entre l'extrémité du cylindre vide (portant le diaphragme) et la face avant du système de garde varie par suite du déplacement de ce système. Nous avons refait l'expérience en gardant cette fois la distance diaphragme système de garde constante, ce qui nous a conduit à déplacer la chambre en sens inverse du système de garde d'une quantité égale. Les mesures alors obtenues ont été corrigées de l'atténuation de l'air sur la distance du déplacement de façon à pouvoir être comparées avec les mesures précédentes.

Le facteur de correction obtenu dans ce second cas, concorde avec celui obtenu dans la première expérience (Fig 7) ce qui met en évidence l'influence négligeable du rayonnement diffusé pouvant provenir du diaphragme ou de la fenêtre de téréphtalate

2 *Déformation du champ électrique par des différences de potentiel entre plaque de mesure et plaques de garde* L'influence de ces différences de potentiel a été déterminée en portant la plaque de mesure (en position moyenne $l = 17$ mm) par rapport aux plaques de garde à des potentiels v situés entre $\pm$ 150 mV et $\pm$ 1,5 volts

Pour une valeur donnée V de la tension de collection la plaque de mesure est portée successivement a un potentiel $+ v$ puis au potentiel $- v$ par rapport aux plaques de garde On a mis en évidence le fait que le rapport

$$\frac{I}{I_{-v}}$$

des courants d'ionisation correspondants est une fonction sensiblement linéaire de v/V (Fig 8), a condition que V soit tel qu'il y ait saturation dans la chambre d'ionisation

En imposant un potentiel v a la plaque de mesure l'on a ensuite mesure les courants d'ionisation I_V et I_{-V}, correspondants a des valeurs de la haute tension égale a $+$ V et $-$ V Après avoir corrigé les valeurs v d'une quantité due a une différence de potentiel de contact, les rapports $\frac{I_V}{I_{-V}}$ se placent sur la droite déterminée plus haut (Fig 8) Il est donc intéressant de déterminer l'erreur due a une éventuelle différence de potentiel de contact en mesurant les courants d'ionisation correspondant à des potentiels de collection $+$ V et $-$ V les plus faibles possible compatibles avec la saturation

C Influence des photons diffusés

La détermination exacte d'une dose d'exposition en roentgens requiert la connaissance de l'ionisation due aux électrons produits par les photons diffusés hors du faisceau primaire ionisation qui doit être déduite de celle mesurée dans la chambre

D'après une technique mise au point par WYCKOFF (15), nous avons effectué les mesures de la contribution des photons diffusés à l'aide de tuyaux de téréphtalate de polyéthylène glycol de 12 mm de diamètre d'épaisseurs différentes alignés coaxiallement avec le faisceau de diamètre 4 5 mm

L'épaisseur des parois de ces tuyaux doit être supérieure au parcours dans le téréphtalate, des électrons primaires Un de ces tuyaux est rendu conducteur par une application d'une mince couche de graphite colloïdal il possède alors une épaisseur de 6 9 μ et peut être porté au potentiel milieu du système de

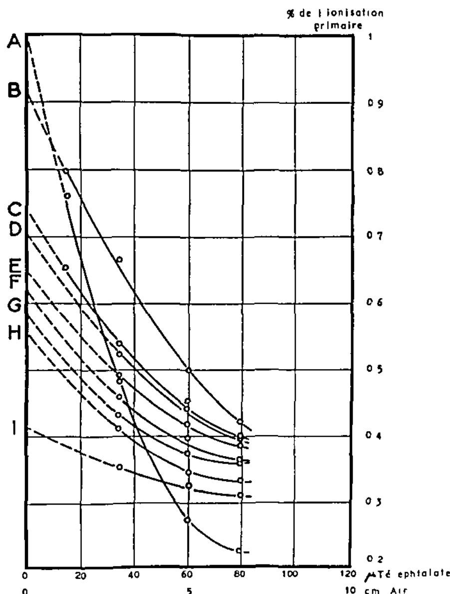


Fig. 9. Variation de l'ionisation relative due aux photons diffusés en fonction de l'épaisseur des tuyaux de téréphtalate.

garde. On peut y insérer d'autres tuyaux de teréphtalate non graphités, d'épaisseurs croissantes (20 μ, 45 μ et 65 μ), ce qui permet de déterminer l'ionisation due à la diffusion en fonction de l'épaisseur. Nous avons auparavant déterminé la valeur de la distorsion du champ électrique causée par le tuyau de teréphtalate. Pour cela nous avons irradié entièrement la chambre à l'aide d'une source de radium et mesuré l'ionisation produite avec et sans le tuyau graphité (10). La différence entre les deux mesures se trouve être de 4,5 %.

Pour chaque rayonnement, nous avons établi la courbe donnant le quotient du courant d'ionisation, le tuyau étant en place, par le courant sans tuyau en

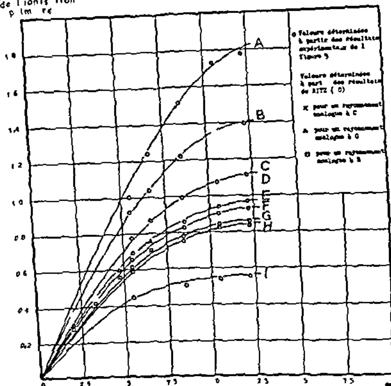


Fig 10 Contribution des photons diffusés dans un cylindre de rayon r centré sur un faisceau de rayons Roentgen de diamètre nul

fonction de l'épaisseur de ce dernier (Fig 9) L'addition des tuyaux de térephtalate revient à augmenter le volume d'air autour du faisceau L'échelle des abscisses de Fig 9 pouvant être convertie en épaisseurs d'air en utilisant le fait que 1 mg/cm² de térephtalate est équivalent à 0 71 mg/cm² d'air (P[43])

Cette courbe extrapolée jusqu'à un diamètre de faisceau nul donne la valeur de la contribution des photons diffusés dans tout le volume de la chambre Il est nécessaire d'introduire une très légère correction pour tenir compte du fait que l'émission électronique du térephtalate est inférieure à celle de l'air Nous avons comparé ces résultats corrigés avec ceux calculés pour notre chambre (qui peut être assimilée à un volume de rayon 5,5 cm) à partir des résultats de RITZ (10)

A partir des courbes de Fig 9 et des résultats de RITZ nous pouvons déduire les courbes donnant le pourcentage de rayonnement diffusé dans un cylindre de rayon donné centré sur le faisceau (Fig 10) Nous avons placé sur ces courbes les résultats obtenus par RITZ (10)

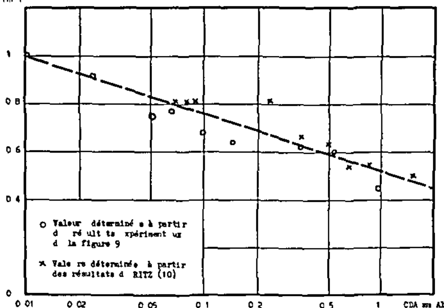


Fig 11 Contribution des photons diffuses dans le volume de la chambre d etude en fonction de la CDA du rayonnement

Nous avons egalement trace (Fig 11) la courbe donnant la valeur de la contribution des photons diffuses dans le volume de la chambre en fonction du logarithme de la CDA du rayonnement utilise Les resultats de Ritz (10) ont ete portes sur le graphique et l accord est satisfaisant

D Saturation

L etude de la saturation a ete faite dans les conditions suivantes 40 kV, 2 mA, filtration additionnelle nulle, la chambre etant placee le plus pres possible du tube a rayons roentgen de façon a obtenir un debit important

Pour une dose d exposition de 126 r/min dans le plan du diaphragme d entree de la chambre, la saturation est obtenue pour 4 500 volts En effet l extrapolation de la courbe $1/i$ en fonction de $1/V$ nous donne une variation du courant d ionisation de 1,4 ‰ lorsque V varie de 4 500 a 9 000 volts ou de 5 000 a 10 000 volts (16)

Ce travail a éte effectué au Laboratoire de Dosimétrie du Service Central de Protection contre les Rayonnements Ionisants dans le cadre de recherches sur les étalons de mesure des doses d exposition Il a pu être réalisé grace a Monsieur le Professeur Bugnard et Monsieur J Massiot nous désirons leur exprimer ici notre vive gratitude

RÉSUMÉ

Les auteurs décrivent une chambre d ionisation a plaques parallèles d un type spécial qui a été utilisée dans les études sur les étalons français de mesure de dose d exposition Cette nouvelle chambre permet la mesure de l ionisation lorsque la longueur de l électrode de mesure

tend vers zéro Le dispositif décrit a permis de mesurer les divers facteurs de correction utilisés dans la determination absolue des doses d exposition en particulier l atténuation de l air les déformations du champ électrique l influence des différences de potentiel de contact ainsi que la contribution des photons diffusés

SUMMARY

A special type of free air ionization chamber is described it was used for investigations on the French exposure dose standard This new chamber enables ionization measurements to be made when the length of the measuring electrode tends toward zero The various correction factors used in the absolute determination of exposure doses were measured using the chamber described especially air attenuation electric field distortions influence of contact potential and scattered photons

ZUSAMMENFASSUNG

Ein besonderer Typus einer Freiluftionisationskammer wird beschrieben Sie ist zur Untersuchung des französischen Bestrahlungsdosisstandards benutzt worden Diese neue Kammer ermöglicht Ionisationsmessungen durchzuführen wenn die Länge der Messelektrode nahezu Null ist Die verschiedenen Korrektionsfaktoren die man bei der absoluten Bestimmung der Bestrahlungsdosis benutzt wurden mit Hilfe der beschriebenen Kammern gemessen insbesondere die Luftschwächung die Störungen des elektrischen Feldes der Einfluss des Kontaktpotentiales und der Streuphotonen

BIBLIOGRAPHIE

1 ALLISY A DELAVERGNE L *and* WYCKOFF *H O* Intercomparison of French and U S roentgen ray standards Acta radiol 48 (1957) 484

2 BUNDE E LANG D LOHLIT W und SEWKOR A Absolute Dosismessung im Gebiet der weichen und sehr weichen Röntgenstrahlung mit Hilfe einer totalabsorbierenden Ionisationskammer *Z* Naturforsch 9a (1954) 129

3 DAY F H and TAYLOR L S Absorption of X rays in air J Res NBS *40 (1948)* 393

4 HÜBNER W Communication personnelle

5 JAEGER R Wahrer und scheinbarer Schwächungskoeffizient inhomogener Röntgenstrahlung Physik Z 36 (1935) 41

6 — Zur Standard Dosimetrie der Grenz und Weichstrahlen Z angew Physik *6 (1954)* 494

7 JENNINGS W A *Beryllium window tube outputs further considerations regarding the* use of constant and pulsating tension *Acta radiol 6 (1951) 477*

8 OOSTERKAMP W J and PROPPER J *Free air and thimble* ionization chambers for Grenz ray dosimetry Acta radiol 37 (1952) 33

9 RAJEWSKY B BUNDE E DORNEICH M et coll Darstellung Wahrung und Übertragung der Einheit der Dosis *fur Rontgen* und Gammastrahlen mit Quantenenergien zwischen 3 keV und 500 keV PTB (1954)

10 *RITZ V H* Design of free air ionization chamber for the soft X ray *region (20—100* kV) Radiology 73 (1959) *911*

11 SOMERWIL A *A grid* ionization chamber of special design for the measurement of soft radiations Acta radiol 37 (1952) 44

12 TAYLOR L S and STONEBURNER C F The measurement of low voltage X ray intensities J Res NBS 9 (1932) 769
13 TROUT F D and GAGER, R M Physical characteristics of soft roentgen rays Amer J Roentgenol 62 (1949), 91
14 VENNART, J Some physical measurements in the grenz ray region Brit J Radiol 27 (1954) 524
15 WYCKOFF H O and KIRN F S Standard chambers requirements for 250 to 500 kV X rays J Res NBS 58 (1957) 111
16 — and ATTIX F H Design of free air ionization chambers NBS Handbook 64 (1957)
17 ZIELER F Zur Charakterisierung weicher Rontgenstrahlung durch Halbwertschicht und Homogenitatsgrad Strahlentherapie 93 (1954) 579
18 — Dosismessungen an Beryllumfenster Rohren fur Spannungen von 10 100 kV Strahlentherapie 100 (1956) 595

REPORT OF THE

INTERNATIONAL COMMISSION ON RADIOLOGICAL UNITS AND MEASUREMENTS

Committee on the Methods of Evaluating Radiological Equipment and Materials Subcommittee on Focal Spots

Report of the Subcommittee IV

1 — Method of Focal Spot Image Formation and Measurement

Introduction

At the 1956 meetings of the International Commission on Radiological Units and Measurements a new committee was established to study methods of evaluating radiological equipment and materials It operates under the Chairmanship of Dr B COMBEE of the Netherlands with Dr E D TROUT of the U S A as Vice Chairman A series of subcommittees have been set up to deal with specialized subjects The report to follow is the first of the subcommittee reports to be completed

As problems of radiation units and measurements have developed during recent years it has become increasingly evident that it is not feasible for the ICRU to publish a regular triennial report covering all areas of interest to the Commission Therefore it has been decided that as different committees or subcommittees of the Commission complete their reports they will be released for whatever Journal publication may appear to be appropriate Approximately every three years the committee will endeavor to compile as many of these reports as possible into a single report By this procedure it is hoped to avoid holding up the release of one completed study simply to have it included in a single report with all other studies

This report of Subcommittee IV of the ICRU is the first such report to be released in the manner described above It will also be included as Appendix IV in the triennial report of the ICRU due for publication within a few months

Committee IV of the ICRU consists of the following members

B COMBEE Chairman Netherlands E DALE TROUT (Vice Chairman) U S A E ZIELER (Technical Secretary) Germany H BERGER Germany BERNARD O LOUGHLIN U S A A S JOHNSTONE England J MASSIOT France D J STEVENS Australia S W SMITH U S A C W WEGELIUS Sweden

The Subcommittee (IV—1) that prepared this specific report consists of the following members

T ROGERS (Chairman) U S A G M ARDRAN England E FENNER Germany R GRIFFOLL France A KUNTKE Germany

This report has been reviewed and approved by the ICRU

LAURISTON S TAYLOR

Chairman International Commission on Radiological Units and Measurements

The task of this Subcommittee has been considerably simplified by the instruction given to it in the report of ICRU IV dated August 14 1958, as follows

Only the tools for making an accurate measurement under any desired operating conditions should be specified The specification of tolerances allowable from nominal focal sizes of the tube current and voltage conditions should be considered to be outside the scope of ICRU IV

Consistent with this instruction, the Subcommittee has given special attention to methods of measurement of focal spot size in X ray tubes for diagnosis In this report we submit our recommendations for a measurement method and procedure suitable for such tubes particularly of the line focus variety when operated at voltages not exceeding 150 kvp

At the ICRU meeting held in Geneva September 1958 it was suggested that Subcommittee 1 should also include in its task the method of measurement of uniformity of focal spots and that the studies should not be limited to diagnostic tubes but should include therapy tubes and possibly radioactive sources The Subcommittee has not as yet been able to evaluate this suggestion It is of the opinion however that a method applicable specifically for diagnostic tubes can and should be recommended at this time and that therapy tubes and radioactive sources should be the subject of further deliberation

The following recommendations represent a composite of the positions taken by the individual members of the Subcommittee with respect to the various points involved rather than the unanimous opinion of all However, a majority are in agreement that the method proposed will give a substantially accurate measure of the effective focal size of an X ray tube under the operating conditions obtained at the time the measurement is made

RECOMMENDATIONS

Method of Focal Spot Image Formation and Measurement
(For diagnostic tubes at voltages up to 150 kvp)

1 *Basic method* Pinhole radiograph of focal spot produced by pinhole accurately aligned with respect to central ray of X ray beam

2 *Details of pinhole camera*

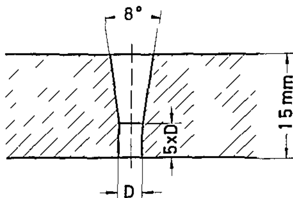
a Pinhole diameter

0 030 mm for focal sizes below 1 0 mm

0 075 mm for focal sizes 1 0 mm to 2 5 mm

0 100 mm for focal sizes above 2 5 mm

b Diaphragm thickness material and pinhole profile The pinhole diaphragm shall be manufactured from a 90/10 gold platinum alloy 1 5 mm thick The cylindrical part of the pinhole shall be five times as long as its diameter and followed by a conical part with a divergent angle of 8 (See diagram below)



c Focal spot to pinhole distance 10 cm minimum (where focus location is not precisely known or directly measurable precise location stereoscopically with dual pinholes is recommended)

d Enlargement factor 2 0 minimum for focal sizes up to 2 5 mm 1 0 minimum for focal sizes above 2 5 mm

3 *Photographic technique*

a Type of film any commonly used dental film (single coating)

b Image density 0 6 to 1 0 as measured in the most dense portion of the image Density to be controlled by means of standard developing technique and proper exposure time at tube current and voltage factors employed (This element involves a point of special difficulty because of variations in structure of respective focal spots If lines in focal spot are superimposed greater maximum density results than in cases where lines are not superimposed for equal exposure values Hence a wide latitude in allowable maximum density becomes necessary)

4 *Measurement of image*

a Lighting Back lighted at approximately 90 foot-candles

b Measurement procedure Use scaled magnifier with 0 1 mm scale divisions 5 to 10 times magnification Measure length and width respectively including all perceptible portions of the image to nearest 0 1 mm For irregularly shaped (non rectangular) focal spots measurement should be taken of all significant dimensions

c Correction of image measurements All image dimensions shall be divided by the enlargement factor accurately determined (see 2 d)

5 *Statement of dimensions*

a Width of focal spot shall be stated as the width of the image divided by the enlargement factor

b Length of focal spot shall be stated as the length of the image divided by the enlargement factor further corrected by a multiplier of 0 7 (See appendix A for explanation)

c For non rectangular focal spots all significant dimensions including maximum diameter shall be stated as indicated by actual measurements divided by the enlargement factor

APPENDIX A

The proposal of a fractional multiplier for correction of the measured image length arises from the long recognized fact that the lengthwise distribution of energy in the focal spot of line focus tube tend to be peaked at the center and diminishes gradually to zero at the ends Hence the effective length based on its effect on either radiographic definition or loading capacity cannot be stated as equal to the measured image length as initially corrected Some further correction is necessary This point has been exposed and to some extent explored in the papers heretofore presented by POLANSKY and O CONNOR (1954) ROGERS (1956) FENNER and JOCHIM (1957) and SERVAIS (1958) However we do not feel that work done to date has been sufficiently comprehensive to establish a suitable correction factor and the suggestion above of a multiplier of 0 7 is given primarily by way of example or as an approximate value rather than as a final recommendation We would like to recommend that ICRU IV enlist the good offices of a suitable research organization to explore this matter quantitatively over the entire range of diagnostic tubes commercially produced with the objective of establishing a proper formula for focal spot length

APPENDIX B Off Focus Radiation

It must be recognized that the effect of any off focus radiation on definition is not taken into account by these measurements and unless off focus radiation is suppressed the definition to be expected from the tube may be influenced by it

REFERENCES

FENNER E und JOCHIM H Bestimmung der Brennfleckgroße aus der geometrischen Unscharfe Fortschr Rontgenstr 87 (1957) 109

POLANSKY D and O CONNOR D T X ray focal spot measurement Nondestructive Testing 12 (1954) 1

ROGERS T H Definition and measurement of the focal spot size of an X ray tube Presented Eighth International Congress of Radiology Mexico City July 24 1956

SERVAIS J Le contrôle des foyers d émission dans les tubes radiogènes et relation entre la largeur de foyer et la netteté relative des images radiographiques J Radiol Electrol 39 (1958) 383

BOOKS RECEIVED

We acknowledge with thanks under this heading books received for review which we trust will be regarded as a sufficient mark of appreciation of the courtesy of the sender The reviews of selected items will appear as soon as opportunity affords

ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS Vol VII Editors Cornelius A Tobias and John H Lawrence Academic Press New York 1960

AUFDERMAUER MAX Die Spondylosis cervicalis (Die Wirbelsaule in Forschung und Praxis Band 17) Hippokrates Verlag Stuttgart 1960

BENTZEN NIELS Urethrographic studies of prostatic tuberculosis Thesis University of Copenhagen 1960

BIAGINI CARISSIMO BOMPIANI CARLO & PALEANI VETTORI PIERO G Le radiazioni di alta energia Basi fisiche e biologiche delle applicazioni terapeutiche Societa Editrice Universo Roma 1960

BOHLIG H JACOB G & MULLER H Die Asbestose der Lungen Genese — Klinik — Rontgenologie Georg Thieme Stuttgart 1960

(THE) CELL NUCLEUS Proceedings of the 1959 Meeting at the University of Cambridge by the Faraday Society Butterworth London 1960

CRONKITE EUGENE P & BOND VICTOR P Radiation injury in man Its chemical and biological basis Pathogenesis and therapy Charles C Thomas Springfield Ill 1960

DAVIDSEN H GOSTA Atrial septal defect An investigation into the natural history of congenital heart disease Munksgaard Copenhagen 1960

DIAMOND HENRY D Die interne Krebstherapie (The medical management of cancer) Deutsche Übersetzung von P Obrecht und P Berg Georg Thieme Stuttgart 1960

DI RIENZO S & WEBER H H Radiologische Exploration des Bronchus Georg Thieme Stuttgart 1960

ECOIFFIER J La radiculographie lombaire dans la sciatique Masson Paris 1960

ERGEBNISSE DER WIRBELSAULENFORSCHUNG (Die Wirbelsaule in Forschung und Praxis Band 15) Zusammengestellt von Herbert Junghanns Hippokrates Verlag Stuttgart 1960

ETTER LEWIS E Glossary of words and phrases used in radiology and nuclear medicine Charles C Thomas Springfield Ill 1960

FELSON BENJAMIN Fundamentals of chest roentgenology W B Saunders Philadelphia 1960

FRIMANN DAHL J Roentgen examinations in acute abdominal diseases Second edition Charles C Thomas Springfield Ill 1960

HEALTH PHYSICS Vol I Progress in nuclear energy (PNE) Series XII Second International Conference on the peaceful uses of atomic energy Editors W G Marley and K Z Morgan Pergamon Press Oxford 1960

HOSLI P O Anomalien der Harnwege im Kindesalter und ihre chirurgische Behandlung S Karger Basel 1960

KAINDL, F MANNHEIMER E PFLEGER SCHWARZ L & THURNHER B Lymphangiographie und Lymphadenographie der Extremitaten Georg Thieme Stuttgart 1960

KLINISCHE NEURORADIOLOGIE Herausgegeben von K Decker Georg Thieme Stuttgart 1960

KUNZLER RALPH & SCHAD NIKOLAUS Atlas der Angiokardiographie angeborener Herzfehler Georg Thieme Stuttgart 1960

LOW LEVEL IRRADIATION Symposium Editor Austin M Brues American Association for the Advancement of Science Washington D C 1960

MAISIN HENRI Contribution a l étude du syndrome médullaire apres irradiation Étude expérimentale Éditions Arscia Bruxelles 1959

MALLET, L La lumière bleue J B Baillière et Fils Paris 1960

MECHANISMS IN RADIOBIOLOGY Vol II Multicellular organisms Editors Maurice Errera and Arne Forssberg Academic Press New York 1960

MEDICAL PHYSICS Vol III Editor Otto Glasser The Year Book Publishers Chicago 1960

MITCHELL J S Studies in radiotherapeutics Harvard University Press Cambridge Mass 1960

NÈGRE A & ROUQUET F Précis de technique radiologique 4 édition G Doin & Cie Paris 1960

PISANI G MALARSINA A & SAVINO G Diagnostica radiologica del cancro della mammella Minerva Medica Torino 1960

RAYONS X RADIO ISOTOPES ET E E G DANS L ÉPILEPSIE Ouvrage publié par les soins de H Fischgold et H Gastaut Masson Paris 1960

RECUEIL PÉRIODIQUE ENCYCLOPEDIE MEDICO CHIRURGICALE 13—14 cahier spécialisé radiodiagnostic Tomes I et II Éditions Techniques Paris 1960

REPORT OF COMMITTEE II ON PERMISSIBLE DOSE FOR INTERNAL RADIATION (1959) ICRP Publication 2 Pergamon Press Oxford 1960

RIESSBECK KARL HEINZ Zur Methodik der Rontgenstrahlen Behandlung bosartiger Geschwulste Zweite erweiterte und neubearbeitete Auflage Georg Thieme, Stuttgart 1960

RODRIGUES DIRCEU Broncografia con bario e metilcelulose Observacoes no henem e estudo experimental Dr Dirceu Rodrigues Rua Almirante Gonçalves 1865 Parana Curitiba 1960

ROUX HENRY Notions de radiobiologie Masson Paris 1960

SCHMIDT HERMANN & FISCHER ERICH Die okzipitale Dysplasie Georg Thieme Stuttgart 1960

SELMAN JOSEPH The basic physics of radiation therapy Charles C Thomas Springfield Ill 1960

SFIRKO SISTER CHRISTINA Radiologic records Charles C Thomas Springfield Ill 1960

TALAIRACH J DAVID M TOURNOUX P CORREDOR H & KVASINA T Atlas d anatomie stéréotaxique Repérage radiologique indirect des noyaux gris centraux des régions mésencéphalo sous optique et hypothalamique de l homme Masson Paris 1959

TURANO LUIGI & SALOMONI ENZO Fisioradiologia dell esofago Normale e patologica Societa Editrice Universo Roma 1960

WACKENHEIM A Neuroradiologie Radio anatomie normale et pathologique du crâne G Doin & Cie Paris 1960

YEAR BOOK OF RADIOLOGY 1959—1960 Series The Year Book Publishers Chicago 1960

ZIMMER E A Filmfehler in der Rontgenpraxis Artéfacts et conséquences d erreur de manipulation sur le cliché radiographique Georg Thieme Stuttgart 1960

ACTA RADIOLOGICA

EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE NORVEGIAE ET SUECIAE

VOL 55 FEBRUARY 1961 FASC. 2

PRIMARY CHONDROSARCOMA OF BONE

by

Å Lindbom G Soderberg and H J Spjut

The histologic diagnosis of chondrosarcoma of bone is difficult and rests upon an appreciation of the subtle morphologic criteria of well differentiated forms of cartilaginous tumors most chondrosarcomas are well or moderately well differentiated The majority of chondrosarcomas are so situated that adequate surgical treatment may mean loss of part or the whole of a limb and at times hemipelvectomy a correct diagnosis therefore becomes of the greatest importance A group of essentially untreated biopsy proved chondrosarcomas and a group that was surgically treated are described and discussed with special reference to the evolution and course of the tumour

Thirty nine cases of chondrosarcomas from the bone tumor registry of Karolinska Sjukhuset have been studied from the clinical pathologic and roentgenologic standpoints and carefully investigated so as to exclude osteo sarcomas benign cartilaginous tumors and the benign tumors that may be confused with chondrosarcomas Sixteen of the cases received no surgical treatment for various reasons e g pathologic underestimation of the malignancy of the tumor age poor health or reluctance to carry out radical surgical procedures all of the 16 received irradiation therapy The tumors of the re maining 23 cases were treated surgically either by local removal or amputation of the affected part 9 of these cases also received irradiation therapy either

From the Institute of Radiopathology (Director Prof Lars Santesson) and Roentgendiag nost c Department D (Director Docent Å Lindbom) Karolinska Sjukhuset Stockholm Sweden Submitted for publication 3 August 1960



a b

Fig 1 a) Peripheral chondrosarcoma grade II in man aged 68 arising in large osteochondroma in proximal metaphysis of humerus b) Invasion of proximal end of humerus by tumor after curettage

preoperatively, postoperatively, or both All of the 39 cases were followed for at least five years or until death

Of the 39 patients, 25 were male and 14 were female The average age of onset of symptoms for the entire group was 46 years, with an age span of 15 years to 84 years The average age differs between the men and the women, being 51 and 36 years respectively For the patients with peripheral tumor the mean age was 38 years and for the patients with central tumor it was 52 years

As in other reported series (DAHLIN & HENDERSON, JAFFE, O NEAL & ACKERMAN) of chondrosarcomas the majority of the tumors in our cases involved the long bones, especially the femur, and the bones of the pelvis (Table 1) Two of the chondrosarcomas arose in the bones of the hand, a phalanx of an index finger and a metacarpal These two cases have been reported in detail previously (JACOBSSON & SPJUT) 1960 Most chondrosarcomas may be classified as central or peripheral, a designation suggesting an origin within a bone or in a peripheral part or surface of a bone In either case the sarcoma may have arisen de novo or from a pre existing benign cartilaginous tumor It is commonly difficult satisfactorily to demonstrate the latter event (Fig 1) Among our cases there were 20 central tumors, 13 peripheral tumors and 6 that were uncertain The classification as to a central or peripheral location was based mainly upon the roentgenographic findings Central chondrosarcomas predominate in some groups (JAFFE) and peripheral in others (O NEAL & ACKERMAN)

Table 1

Location of tumor in surgically treated and untreated patients

Site	Treated Central	Treated Peripheral	Treated Unknown	Untreated Central	Untreated Peripheral	Untreated Unknown	Total
Acetabulum	2	1	—	1	—	—	4
Ilium	—	3	—	4	2	1	10
Tibia	1	—	—	—	—	—	1
Femur	5	1	—	3	1	—	10
Humerus	—	—	—	1	1	—	2
Scapula	1	—	1	—	—	—	2
Hand	1	1	—	—	—	—	2
Sternum	—	—	—	1	—	—	1
Pubis	—	1	—	—	—	1	2
Sacrum	—	1	—	—	—	—	1
Ribs	—	1	2	—	—	—	3
Vertebra	—	—	1	—	—	—	1
Total	10	9	4	10	4	2	39

The major signs and symptoms may be seen in Table 2. It may be noted that 24 of the patients complained of pain at some period. Frequently the pain was not severe or persistent but occasionally patients had pain that gradually became severe enough to be incapacitating. All but three of the patients had evidence of a mass or swelling in the region of the tumor; among the peripheral chondrosarcomas a mass was frequently the only symptom. That chondrosarcoma has a rather long clinical evolution is well known (DAHLIN & HENDERSON; JAFFE; O'NEAL & ACKERMAN; and LICHTENSTEIN). Patients may have noted a slowly enlarging mass or pain for years before medical attention is sought. The dating of the onset of symptoms was often inexact. Two of the patients' tumors were discovered incidentally, one during an injection and one during puerperium. The duration of symptoms prior to diagnosis was approximately the same for patients having central and peripheral chondrosarcoma.

Table 2

Signs and symptoms in the material classified according to site

	Central lesion	Peripheral lesion	Unknown site	Total of cases
Pain	16	4	4	24
Stiffness or pain on movement	7	—	2	9
Muscle atrophy	5	—	—	5
Tumor or swelling	18	12	6	36
Tenderness	3	—	2	5
Fluid in joint	1	—	—	7
Local temperature	1	—	1	2



Fig. 1. a) Peripheral chondrosarcoma grade II in man aged 68 arising in large osteochondroma in proximal metaphysis of humerus. b) Invasion of proximal end of humerus by tumor after curettage.

pre-operatively, postoperatively, or both. All of the 39 cases were followed for at least five years or until death.

Of the 39 patients, 25 were male and 14 were female. The average age of onset of symptoms for the entire group was 46 years, with an age span of 15 years to 84 years. The average age differs between the men and the women, being 51 and 36 years respectively. For the patients with peripheral tumor the mean age was 38 years and for the patients with central tumor it was 52 years.

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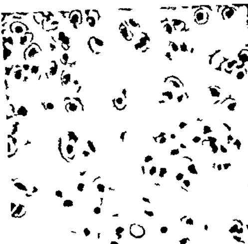


Fig 3



Fig 4



Fig 5

Fig 3 Central chondrosarcoma grade II of femur Somewhat more cellular than grade I Plump nuclei binucleate cells present Treated by irradiation only Patient died two years after biopsy confirmation of tumor Hematoxylin and eosin × 220

Fig 4 Chondrosarcoma grade III of ilium Bizarre nuclear and cellular pattern Irradiation therapy after biopsy Patient died after two years Hematoxylin and eosin × 220

Fig 5 Embolus of chondrosarcoma grade III in artery Primary tumor centrally in femur in a girl aged 16 Disarticulation of hip after biopsy Died three and a half years later with pulmonary metastases and numerous arterial emboli of chondrosarcoma Hematoxylin and eosin × 35

lesions this is not necessarily a measure of the potential of the tumor but possibly a reflection of the adequacy of removal However it does seem to indicate some vigor on the part of the tumor

The grading of our cases was based upon the criteria of O NEAL & ACKERMAN (Table 3) Since 16 of the patients had biopsies only the material for grading was not always generous and consequently the grading in these cases may not reveal the potential of the entire tumor Nineteen of the cases (50 %)

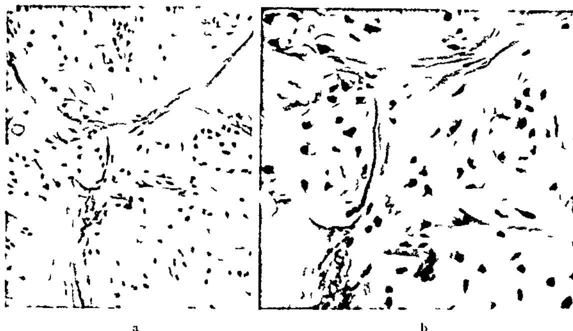


Fig. 2. Chondrosarcoma grade I of vertebra. Plump nuclei and occasional binucleate cells. Three recurrent tumors curetted. Irradiation therapy given. Patient alive after 15 years. van Gieson a) × 90 and b) × 220.

Pathology. The malignant component of chondrosarcoma is cartilaginous whereas in the chondroblastic type of osteosarcoma, malignant cartilage is associated with malignant bone and osteoid and a malignant stroma. These two conditions can ordinarily be separated microscopically. The problem revolves around defining criteria for the well differentiated chondrosarcoma. It is among the well differentiated lesions that an erroneous diagnosis is most common. The criteria used are those described by LICHTENSTEIN and JAFFE. The validity of the criteria has been supported by others, notably O'NEAL & ACKERMAN and DAHLIN & HENDERSON. The criteria are (1) many cells with plump nuclei, (2) more than an occasional cell with two such nuclei, (3) giant cartilage cells with large single or multiple nuclei or with clumped chromatin. Variations as to quantity of the cell alterations plus the presence or absence of calcification and enchondral ossification form the basis for grading chondrosarcomas (O'NEAL & ACKERMAN (Figs. 2, 3, 4) (Table 3)).

Our findings when using the above mentioned criteria confirm those of other observers, i.e. that the well differentiated chondromatous tumors with the nuclear aberrations described are indeed malignant neoplasms capable of invasion, destruction, recurrence and of distant metastases. It is true that the number of patients with known metastases in our group is small, 8 out of 39, but two of the cases with metastases had well differentiated chondrosarcoma (grade I). Seven of the 19 grade I chondrosarcomas had recurrent



Fig 7 Manubrium of sternum expanded by chondrosarcoma in a man 84 years old



Fig 8 Chondrosarcoma grade II in distal metaphysis of femur in man of 28 Small spotty calcifications indicate nature of process its unusual appearance somewhat suggestive of aneurysmal bone cyst

Five of the patients with metastases had central chondrosarcoma two peripheral and one of unknown classification Four of the patients had received no therapy other than irradiation two had been treated primarily by amputation and two had amputation for locally recurrent tumor

Roentgenographic findings Spotty calcification of the type seen in cartilaginous tumors was observed in 22 of the 39 cases (Fig 6) In 15 of the 22 cases the calcification was so abundant and typical that one could say with a high degree of certainty that the tumor was cartilaginous Periosteal bone formation was noted in 8 of the cases Twenty one cases in all had roentgen evidence of bone destruction the areas of destruction being plainly lobulated in 10 cases (Fig 6) The bone was expanded around seven of the tumors (two of the femur one of the sternum Fig 7 one of the acromion and three of the pelvis) The greatest diameters of the tumors measured from the first films of the tumor varied greatly The largest tumor was a central chondrosarcoma of the femur this tumor measured 30 cm in length The two smallest measured 2 cm



Fig 6 Chondrosarcoma grade I filling out almost the entire diaphysis of femur in a woman aged 44 Lobulated destruction of cortical layer from within and expansion of bone in places Typical spotty calcification centrally in tumor tissue

were regarded as grade I, fourteen (37 %) were grade II, and five (13 %) were grade III The distribution of the grades is similar to that reported by DAHLIN & HENDERSON

The best biopsy provides enough viable tumor tissue upon which a helpful opinion can be rendered This usually means a carefully performed, generous incisional biopsy Among our patients there were 24 who had biopsy prior to therapy, 8 of these were needle biopsies It is possible to establish a specific diagnosis from a study of needle biopsies of cartilaginous tumors and even in the small fragments of tissue the criteria enumerated for malignancy could be found Small portions of richly cellular cartilage with many atypical nuclei were occasionally obtained As with any small biopsy, variation in the pattern of a tumor may often result in an uncertain or benign labelling of malignant growths It must be emphasized that the clinical findings and the roentgenogram are important adjuncts to the diagnosis even when larger fragments of tissue are obtained

Microscopic study of the recurrent lesions failed to reveal any increase in the grade of malignancy as compared to the original tumor The survival time of the patients with and without recurrences is the same, an average after the first tissue diagnosis of 8 3 years for those with recurrences and 8 5 years for those without recurrences This would suggest that in our small group of cases the recurrent lesions had not increased in malignancy and would correlate with our findings by microscopy

Eight (21 %) of the patients had distant metastases, demonstrated either microscopically or macroscopically In all except one of the cases the metastases were in the lungs, the exception was lymph node metastases in the case of a chondrosarcoma of the left humerus In one case several arterial emboli of tumor tissue were produced by the pulmonary metastases (Fig 5) In addition to the eight cases with metastases, one case had direct invasion of the vagina from a chondrosarcoma of the ilium This occurred in a 64 year old woman who died 3 months after diagnosis Removal of the tumor was not attempted

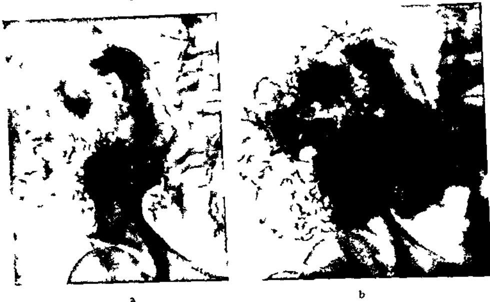


Fig. 9. Chondrosarcoma grade I in wing of ilium in man aged 41. Effect of irradiation. a) Recurrence of tumor after two resections 8 and 4 years earlier. Postoperative defect in ilium. Spotty calcification in recurrent tumor tissue. b) Two years later, after irradiation: calcification of tumor tissue.

local resection possible in many such cases. Chondrosarcoma of the pelvis, on the other hand, is difficult to treat by local resection as it is often impossible adequately to remove the entire tumor and eventually distant metastases may occur. The nature of the condition often gives the surgeon a second or a third chance (LEWIS & PELTIER). Ordinarily hemipelvectomy is the most successful method of treating chondrosarcomas of the pelvic bones. Of the malignant diseases successfully treated by hemipelvectomy, chondrosarcoma is in fact in the forefront (COLEY et coll., TAYLOR & ROGERS, LEWIS & BICKEL).

Twenty three of our patients were subjected to some form of surgical treatment: eight patients had amputation, twelve patients underwent local resection and 3 had local resection followed by amputation. Fifteen of the patients had either pre-operative or postoperative irradiation or both. Benefits, if any, from the irradiation are obscure except as pertain to palliation. Doses varied from 1 600 r air dose to 13 600 r air dose; the treatments were often given in interrupted series. One patient with a grade I peripheral chondrosarcoma of the ilium developed an undifferentiated sarcoma at the site of irradiation some 13 years after initial excision and 5 years after irradiation therapy, a total dose of 12 300 r in four spaced doses having been given. Three recurrent tumors, all chondrosarcoma, had been removed 13 years, 9 years and 5 years

in their greatest diameter and were from the index finger and the acetabulum The chondrosarcoma with the largest mass occurred in the ilium and measured 23 × 15 cm

Evidence of a soft tissue component was seen in 25 of the cases The soft tissue tumor could often be detected because of the presence of calcification, in a few cases the tumor was so large that it was readily seen roentgenographically, contrasting with the surrounding fat In several cases scalloped calcifications outlined the soft tissue component of the chondrosarcoma (Fig 8) This was especially evident in some cases after roentgen treatment (Fig 9)

Sclerosis of bone was observed in 10 cases It was often difficult to determine whether the sclerosis occurred in the bone or was the result of superimposed calcific foci in the tumor

Roentgenographically 13 of the cases were so typical of chondrosarcoma that one could make the diagnosis with certainty Two of the cases occurred in the femoral diaphysis (Fig 6), two involved ribs, and the remainder the pelvis or upper femur Histologically, 10 of these typical cases were considered grade I and 3 as grade II Thus those most roentgenographically characteristic were very well or moderately well differentiated The roentgenograms of the poorly differentiated chondrosarcoma were generally less typical of that tumor

The tumor was not noticed on the first roentgen examination in four of our cases All of these lesions were small Three of the tumors were located in the acetabulum (Fig 10) and the fourth involved a femoral condyle (Fig 11)

Of the 26 cases in which the roentgenographic appearances were considered as being atypical of chondrosarcoma, 12 presented a picture that suggested a malignant tumor of an undetermined type In 9 of these 26 cases some spotty calcifications indicated the possibility of a cartilaginous tumor Approximately a third of all chondrosarcomas seem to have quite typical roentgenographic appearances

Treatment For all practical purposes the treatment of chondrosarcoma is surgical In our experience and in that of others irradiation therapy has proved to be only palliative (Dahlin & Henderson, Jaffe, Haggart et coll) As a general principle in surgical management, biopsy should precede radical treatment With a confirmed diagnosis the proper surgical procedure, based upon location of the lesion in relation to the part of the body, physical state of the patient and microscopic appearances of the tumor, may be undertaken The procedure of choice is one that will entirely encompass the lesion In some instances this may mean hemipelvectomy or amputation but in other cases local resection may suffice A *peripheral chondrosarcoma of the metaphysis of the femur*, for example, may very well be treated by local resection Slow evolution of the tumor and a tendency to local recurrence before metastases appear makes



Fig 11 Small chondrosarcoma grade II of lateral femoral condyle in man aged 39 Poorly delimited destruction and slight periosteal reaction (arrows)

more local recurrences Eight patients were treated primarily by amputation, two of these had local recurrence of the tumor The high frequency of recurrent chondrosarcoma would seem to indicate that the potential of the tumor was not appreciated and the field of excision was consequently unduly conservative The recurrence in itself as already indicated does not necessarily hasten the death of the patient but often the recurrent tumor becomes more and more inaccessible until removal is impossible In terms of 5 years and 10 years survivals the figures for those patients having recurrent chondrosarcoma are nearly the same as for patients without recurrence (61 % 5 years survival and 31 % 10 years survival with recurrent tumor 56 % 5 years survival and 44 % 10 years survival without recurrence)

The group of essentially untreated chondrosarcomas is of special interest From a study of these cases it has become apparent that cartilaginous tumors of long and flat bones judged benign from the insidious progress or lack of microscopic evidence of frank malignancy are often in fact malignant as determined from the course The peripheral lesions of this group are similar



Fig 10 Chondrosarcoma grade I in acetabular region in woman aged 61 a) Healthy side b) Small destruction medially in acetabulum c) After one and a half years slow growth obvious roentgenographic changes Rarefaction 3—4 cm large with destruction of cortical layer d) Another one and a half years later Large tumor growing into pelvis with destruction of pubic bone

before the undifferentiated sarcoma appeared It is possible that the sarcoma represented an undifferentiated form of chondrosarcoma or an irradiation induced sarcoma

The success of a mode of therapy for a malignant neoplasm may be judged not only on long term survival but on recurrences Of our 15 patients treated initially by local resection (curettage not included), 11 (73 %) had one or



a



b



c

Fig 1? C nt al chondrosa coma grade I of humeru in man ag d 5? T eated by curet ta e b opsy followed by irradiation Al e 1? years after biopsy

a) Lobulat d fa ly well d limited destruct on in head of humerus

b Irregi lar bone scleros in tumor reg on three years after treatm nt

Ph tom crograph Hematoxylin and eos n ?80

Table 3

Classification of the material in histologic groups, based upon the criteria of O NEAL & ACKERMAN *indicated by the roman numerals*

Low grade (I)	Moderately malignant (II)	Highly malignant (III)
Occasionally very plump nuclei or general plumping of many nuclei	Many plump nuclei	Great variation of nuclear size and many very plump nuclei
Few double nuclei	Frequent plump double nuclei	Many double nuclei
No multinucleated giant cells	None to rare multinucleated giant cells	Occasional to frequent multinucleated giant cells
Enchondral osteogenesis often irregular	Enchondral osteogenesis bizarre and disorganized	No enchondral osteogenesis
Calcification frequent	Occasional but slight degree of calcification	No calcification

clinically and roentgenographically to those that have been classified as giant osteochondromas or 'extensive osteochondroma' (COLEY) All sixteen patients had a biopsy, from the time of which until death the average length of life was 1 8 years with a time span of 3 months to 14 years If the one survivor is subtracted, the time range of survival is 3 months to 4 years Survival from onset of symptoms until death, with one exception, averaged 4 2 years with a span of 10 months to 14 5 years For comparison the survival times for the patients who had surgical treatment averaged 8 6 years from biopsy to the end of the follow up period and 10 5 years from the beginning of symptoms to the end of the follow up period Four of the 16 cases had known metastases and one had invasion of the vagina As no postmortem examination was performed in most of those patients who died, information as to the actual numbers with metastatic sarcoma or of the extent of the primary tumor, was not obtained

The reason for not giving treatment other than irradiation therapy to these patients was not always clear from the notes Refusal of surgery by the patient, poor physical condition of the patient, reluctance on the part of the pathologist to diagnose chondrosarcoma, the presence of pulmonary metastases, were all reasons for lack of surgical intervention Age was possibly a factor in relation to the physical condition as in this group the average age was 52 5 years, whereas for the treated patients the average age was 41 6 years The location of the lesions in the two groups was similar (Table 1), however, more than half of the 'untreated cases were central types although less than half were central in the surgically treated group The size of the tumor, as determined roentgenographically, did not seem likely to have influenced the type of therapy in most cases In the two groups the average size was the same, 9 2 cm in diameter Histologically, as far as grade of malignancy was concerned, 10 (62 %) were grade I, 3 (19 %) grade II and 3 (19 %) grade III



a



b



c

Fig 12 Cen ral chondro arcon a grade I of hum rus in ma aged 5? Treated by curet tage biopsy f l wed by rradiat on Alive 15 y ars after b opsy

a) Lol ulated fa rl well del m ted destruction in head of humerus

b Irr gul bone sclero is in tumor region three ye rs aft r treatment

c Phot m cr graph Hemato yl n and eo × 280

This compared with 50 % grade I, 37 % grade II and 13 % grade III for the entire group.

All of the 16 patients classified as 'untreated' received irradiation therapy. There was no planned program of irradiation treatment of chondrosarcoma. The patients received from 1 200 r to 18 600 r air dose in the tumor area. Seven of the patients noted no change in symptoms, usually pain, or in the size of the tumor following irradiation. The other patients felt less to no pain after therapy, and three were aware of a decrease in the size of the tumor. All of the palliative effects were temporary except in the one patient who survived 14 years after irradiation; this was a 52 year old man with pain in his right shoulder. Biopsy of the lesion was performed by curettage and several soft cartilaginous fragments were examined and alterations suggestive of chondrosarcoma were noted. The patient received 2 000 r to a posterior field and 2 000 r to an anterior field over the tumor, and three years later additional irradiation was administered to bring the total dose to 5 500 r to the anterior field and 5 100 r to the posterior field. It is not certain whether the curettage, which yielded a fairly small amount of tissue, was sufficient to have removed the lesion. Possibly the combination of the curettage and the irradiation were equally or together effective in producing a 14 years' survival (Fig. 12).

Prognosis. Because of the long course of many chondrosarcomas before and after treatment, and even with inadequate treatment, the standard of 5 years' survival has less meaning than, for example, in osteosarcoma. Figures for 5 and 10 years' survival have been infrequently published. GESCHICKTER & COPELAND reported a 5 years' survival rate after operative treatment of 44 % (38 patients alive and well out of 86).

All of our patients were followed for a minimum of 5 years or until death. The overall 5 years' survival is 38 % (15 patients who lived 5 years). The 10 years' survival is 23 % (9 patients lived 10 years or more). If the three patients who are not as yet eligible for 10 years' survival are not included to calculate the 10 years' survival, the figure is 25 %. The follow up period for these calculations began with the first biopsy or resection. Basing the survival on the entire life history of the chondrosarcoma, the 5 years' survival for our patients is 59 % (23 lived 5 years or more). The 10 years' survival is 26.3 % (10 lived 10 years or more). Of the patients who died, 26 were said to have died with tumor and 5 died without clinical or autopsy evidence of chondrosarcoma. One of the 8 patients alive today has persistent chondrosarcoma, the other seven patients are clinically free from tumor.

The benefit of surgical therapy, even though not always adequate, is evident from the 5 and 10 years' survival figures for our group of 'untreated' cases. Among our patients receiving only irradiation therapy after biopsy, one survived 5 years, the same patient has survived more than 10 years. Thus the 5 and 10 years' survival is 6.2 %. Of the 23 patients treated surgically, 14 (60.9 %),

survived 5 years or more postoperatively Eight patients lived 10 years or more (34 8 %)

From the aspect of anatomic location peripheral or central in bone the patients having chondrosarcomas classified as peripheral have a better 5 and 10 years survival rate than those with central chondrosarcoma The comparative figures are peripheral 5 years survival 53 8 % and 10 years survival 30 7 % the central 5 years survival is 30 % and the 10 years survival 20 % Among the tumors of unknown classification there was one case which survived 7 years and another 15 years Survival related to chondrosarcoma of the axial skeleton (including pelvis vertebra and ribs), or bones of the limbs, shows that the survival percentage is better in cases of chondrosarcoma of the extremities This would be expected The 5 years survival for chondrosarcoma of the extremities is 46 6 % (7/15) the 10 years survival is 33 3 % (5/15) For chondrosarcoma of the axial skeleton the 5 years survival is 33 3 % (8 survivors among 24) and the 10 years survival 16 6 %

Related to the histologic grade of the tumor the results are reverse of what would be expected *i e* the survival was better for grade II as opposed to grade I The 5 years results were 42 % for grade I and 47 % for grade II The 10 years survival percentages were 31 % and 36 % respectively None of the 5 cases with grade III chondrosarcoma survived as long as 5 years

Conclusions

The diagnosis of cartilaginous tumors by microscopy is often difficult and requires considerable experience It is however most important if treatment is to be adequate and satisfactory Our 16 patients who were essentially untreated except for irradiation therapy, illustrate well the outcome of chondrosarcoma under such circumstances The 5 and 10 years survival figures are poor compared to those patients who had some form of surgical therapy

In terms of length of life even poorly performed local resections of chondrosarcomas give good results in the face of local recurrences Well performed resections or amputations with a low recurrence rate do not as our figures indicate give much better 5 and 10 years survival rates Other factors also influenced prognosis in our cases If the lesion was located in a bone of an extremity as opposed to in bones of the axial skeleton the prognosis was more favorable in terms of percentage of 5 and 10 years survival Similarly peripheral chondrosarcomas have a better survival rate than central chondrosarcomas The histologic grade of malignancy was of particular prognostic significance whereas none of the cases with grade III chondrosarcoma survived 5 years

Our study supports previous observations that chondrosarcoma is a slowly progressive tumor both before and after diagnosis However even those that appear to be pathologically and roentgenologically benign are capable of local recurrence and of distant metastases Surgical treatment suited to the location of the lesion is the procedure of choice Except in one case radiation

therapy served only as a temporary palliative of local symptoms. In a few cases the size of the tumor appeared to regress under irradiation.

The overall 5 years' survival rate was 38 % and 10 years' survival 23 %.

SUMMARY

Primary chondrosarcoma of bone was studied in a material of 39 cases. Sixteen of the cases were treated only with irradiation and the 5 year survival rate was 6.2 %. Twenty three patients had either local resection, amputation or both with a survival rate of 60.9 % for 5 years and 34.8 % for 10 years. The overall 5 years survival rate for the 39 patients was 38 % and the 10 years rate 23 %.

ZUSAMMENFASSUNG

Das primäre Chondrosarkom des Skeletts wurde an einem Material von 39 Fällen studiert. Sechzehn der Fälle wurden nur strahlenbehandelt und 6.2 % zeigten eine 5 jährige Überlebenszeit. Dreiundzwanzig Fälle wurden entweder lokal reseziert, amputiert oder beiden Eingriffen unterzogen und 60.9 % von diesen zeigten eine 5 jährige und 34.8 % eine 10 jährige Überlebenszeit. Von allen 39 Patienten lebten 38 % nach 5 Jahren und 23 % nach 10 Jahren.

RÉSUMÉ

Les auteurs étudient le chondrosarcome primitif de l'os sur une série de 39 cas. Seize de ces cas ont été traités uniquement par les radiations avec un taux de survie de 5 ans de 6.2 %. Vingt trois malades ont subi soit une résection locale, soit une amputation, soit les deux, avec un taux de survie de 60.9 % à 5 ans et de 34.8 % à 10 ans. Le taux de survie de 5 ans de l'ensemble des 39 malades fut de 38 % et de 23 % à 10 ans.

REFERENCES

COLEY, B. L.: Neoplasms of bone. Paul B. Hoeber, New York 1949.

— HIGINBOTHAM, N. L. and ROMIEU, C.: Hemipelvectomy for tumors of bone. Amer. J. Surg. 82 (1951), 27.

DAHLIN, D. C. and HENDERSON, E. D.: Chondrosarcoma. A surgical and pathological problem. J. Bone Jt Surg. 38 A (1956), 1025.

GESCHICKTER, C. F. and COPELAND, M. M.: Tumors of bone. Third edition. Lippincott, Philadelphia 1949.

HAGGART, G. E., JOHNSTON, D. O. and CREEDON, F.: Supervoltage radiation for sarcomata of the pelvis and lower extremities. J. Bone Jt Surg. 40 A (1958), 870.

JAFFE, H. L.: Tumors and tumorous conditions of the bones and joints. Lea & Febiger, Philadelphia 1958.

LEWIS, F. J. and PELTIER, L. F.: Multiple planned operations in a patient with residual chondrosarcoma. Cancer 11 (1958), 624.

LEWIS Jr, R. C. and BICKEL, W. H.: Hemipelvectomy for malignant disease. J. Amer. med. Ass. 165 (1957), 8.

LICHTENSTEIN, L.: Bone tumors. Second edition. C. V. Mosby Co., St. Louis 1959.

O'NEAL, L. W. and ACKERMAN, L. V.: Chondrosarcoma of bone. Cancer 5 (1952), 511.

JAKOBSSON, F. and SPJUT, H. J.: Chondrosarcoma of the bones of the hand. Acta radiol. 54 (1960), 426.

TAYLOR, G. W. and ROGERS Jr, W. P.: Hindquarter amputation. New Engl. J. Med. 249 (1953), 963.

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ROENTGEN EXAMINATION OF THE INFERIOR VENA CAVA IN CHRONIC HEPATIC DISEASE

by

OLAF PETERSEN NIELS TYGSTRUP and KJELD WINKLER

Pressure measurements in the central veins in cirrhosis of the liver have shown that a pressure gradient exists between the abdominal and thoracic part of the inferior vena cava in about one third of cases (WINKLER TYGSTRUP & HANSEN 1960) The gradient usually occurred centrally to the outlet of the hepatic veins at the level of or just below the diaphragm The present study was carried out in order to assess if this gradient could be attributed to narrowing of the infra diaphragmatic part of the inferior vena cava

Roentgen examination of the inferior vena cava with injection of contrast media has been widely used particularly for demonstration of retroperitoneal tumours (dos SANTOS 1935 O LOUGHLIN 1947 OLIVIER 1951 HELANDER & LINDBOM 1956 1959) but generally only the caudal part of the vein i e the part below the renal veins has been examined There is little information about the configuration of the upper course of the inferior vena cava VIALLET et coll (1957) have described a more or less marked compression of the intrahepatic part of the vein in Algerian children with hepato splenomegaly and a paper by FARINAS (1947) contains an illustration showing a constriction of the vein in a patient with hepatic cirrhosis

Submitted for publication 27 June 1960

Table

Survey of material

No	Age	Sex	Clinical condition	Smallest area of inf vena cava as a percentage of supradiaphragmatic area	Pressures in mm Hg	
					Right atrium	Inf vena cava
1	16	f	Normal	8[illegible]	5	[illegible]
2	17	m	Normal	49	3	5
3	[illegible]0	m	Bronchial asthma	61	3	4
4	17	f	Normal	2[illegible]	4	5
5	[illegible]1	m	Chronic bronchitis	10	5	7
6	57	f	Cirrhosis	20	3	[illegible]
7	54	m	Cirrhosis	24	10	16
8	53	f	Cirrhosis	10	5	6
9	5[illegible]	m	Fatty liver	9	8	13
10	63	m	Cirrhosis	37	4	[illegible]

Material and Methods

The diagnoses of the cases are given in the Table above. Cases 1 to 5 had no clinically demonstrable hepatic disease, and in Cases 6 to 10 the diagnoses were confirmed by liver biopsy. In the cases of cirrhosis the condition was at an advanced stage, but ascites, when present, did not noticeably distend the abdominal wall. Case 9 (with fatty infiltration of the liver due to chronic alcoholism) had a large liver and moderately abnormal liver function tests.

The patients were premedicated by 200 mg of phenobarbitone; apart from this no anaesthesia was given. The examination was performed with the patients supine. A Lehman catheter was introduced via an antecubital vein into the inferior vena cava with the tip at the level of Th 12, i. e. below the outlet of the hepatic veins, and 33 to 40 ml Urografin® 76 % were injected with an automatic pump (Gidlund) during 3 seconds. Five exposures in the antero-posterior and lateral planes were made at intervals of one second. The patients were instructed to stop breathing during the exposures (without Valsalva manoeuvre). The injection was generally accompanied by a momentary burning but not painful sensation in the upper abdomen; apart from this no side reaction was observed. The pressure measurements listed in the table were performed with the Lybjærg Hansen condenser manometer as previously described (WINKLER et coll. 1960).

Results

The inferior vena cava from the level of the renal veins to the right atrium is clearly outlined with the technique employed. This is largely due to the fact that the contrast medium is injected against the blood flow in the vein so that the contrast medium and blood are thoroughly mixed. No backflow of the medium to the hepatic veins was observed; on the contrary, dilution of the contrast medium by hepatic venous blood was frequent. Care must be taken



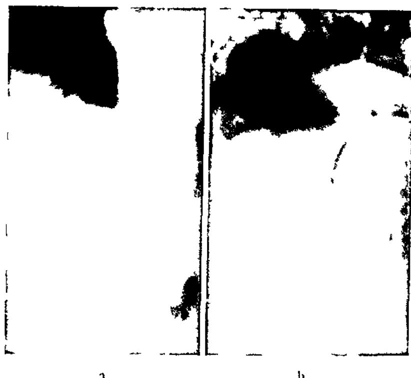
Fg 1 Normal ca a) A p G adual d minution of the lumen of the infe ior vena cava from the enal veins to the diaph agm The l men of the sup adiaph agmat c part of the ein again increa ses and rema ns con tant unt l the vein enters the ight atrium b) Lateral Only small alte t ons in ze a seen There i no reflux of con trast med um into the hepat c ve ns

Fg 2 Hepatic c rrhosis a) A p Considerable dec ease in size of the vena cava at the level of the d aph agm b) Lateral. The constrict on is le s marked The contours of the vein ju t below the d aphragm are not sharp anteriorly due to mixing with blood f ee of contrast medium from the hepatic vein

not to mistake this phenomenon for a narrowing of the lumen Contraction of the inferior vena cava during the atrial systole as described by KJELLBERG & OLSSON (1954) could not be demonstrated

In the subjects with a normal liver the diameter of the inferior vena cava in the antero posterior projection gradually decreases from the level of the renal veins to the diaphragm above which it again increases to remain constant to the point where the vein enters the right atrium (Fig 1a) The same con figuration but generally less evident could be seen in the lateral projection (Fig 1b) The degree of narrowing varied greatly in the subjects studied In the patients with disease of the liver this narrowing appeared to be accentuated, in some of the cases it was most clearly seen in the a p view (Fig 2) and in others in the lateral projection (Fig 3)

The transverse sectional area of the inferior vena cava at different levels was calculated from the diameters in the a p and lateral projections presuming the transverse section to be elliptical when the diameters were different In order to compare the degree of narrowing from case to case the sectional area of the abdominal part of the inferior vena cava was expressed as a percentage of the



a b

Fig 3 Hepatic cirrhosis a) A p Only an insignificant constriction of the inferior vena cava is evident b) Lateral A marked diminution in size near the diaphragm is now apparent

area of the thoracic part (the Table and Fig 4) The Table shows that the individual variation is considerable, although, if the average values of the normal subject and of those with hepatic disease are compared, a true difference can be demonstrated The smallest area as a percentage of the area of the thoracic part was in the cases with a normal liver 36 % and in the cases of hepatic disease 18 %

Discussion

Interpretation of the results is difficult because no definite limit between the narrowing of the sub diaphragmatic part of the inferior vena cava in cases with and without hepatic disease could be demonstrated However, as this narrowing is more constant and generally more marked in the cases of liver disease, it appears justifiable to consider it at least contributory to the ab domino thoracic venous pressure gradient frequently observed in this condi tion

The etiology of the narrowing is not elucidated by this study It may equally well be due to compression of the intra or retro hepatic part of the vein, e g caused by regeneration nodules in the fossa venae cavae of the liver, and to

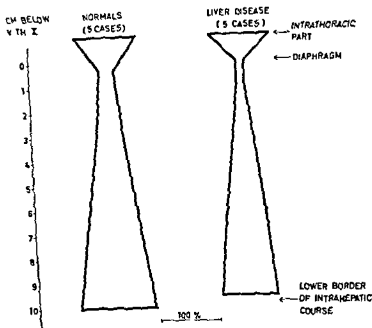


Fig 4 Average horizontal cross section areas of the inferior vena cava in normal individuals and patients with liver disease

increased intra abdominal pressure i e a functional stenosis In the present material ascites in sufficient amounts to cause increased pressure in the abdominal cavity was not present and in our opinion the first mentioned hypothesis seems to be the more acceptable The material presented is too small to show whether there is a correlation between the pressure gradient and the narrowing as shown by cavography with the present technique for this purpose further standardization of the method and determination of the inferior caval blood flow would appear to be necessary

The significance of increased pressure in the inferior vena cava in the pathogenesis of portal hypertension and ascites has been previously discussed (WINKLER TYGSTRUP & HANSEN 1960)

SUMMARY

Angiographic examination of the inferior vena cava in 5 cases of chronic hepatic disease and 5 normal controls have shown that narrowing of the vein just below the diaphragm was more marked in the former group This may be caused by pressure exerted by the diseased liver on the intra or retro-hepatic part of the vein and may partly account for the increased abdomino-thoracic venous pressure gradient described in cases of cirrhosis

ZUSAMMENFASSUNG

Angiographische Untersuchungen der Vena cava inferior in 5 Fällen mit chronischer Lebererkrankung und in 5 normalen Kontrollfällen haben gezeigt, dass eine Verengung der Vene unmittelbar unter dem Zwerchfell in der ersten Gruppe deutlicher markiert war. Dieses kann durch den Druck verursacht sein, der von der erkrankten Leber auf den intra- oder retrohepatischen Teil der Vene ausgeübt wird, und kann teilweise den erhöhten abdomino-thorakalen venösen Druckgradient erklären, der in Fällen mit Zirrhose beschrieben wird.

RÉSUMÉ

L'examen angiographique de la veine cave inférieure dans 5 cas d'affection hépatique chronique et chez 5 témoins normaux a montré que le rétrécissement de la veine juste au dessous du diaphragme est plus marqué dans le premier groupe. Ceci peut être dû à la pression exercée par le foie pathologique sur la partie intra- ou rétro-hépatique de la veine et peut expliquer en partie l'augmentation du gradient de pression veineuse abdomino-thoracique constatée dans des cas de cirrhose.

REFERENCES

Dos Santos, R. Phlébographie de la veine cave. J. Urol. méd. chir. 39 (1935), 586.

Farinas, P. L. Abdominal venography. Amer. J. Roentgenol. 58 (1947), 599.

Helander, C. G. and Lindbom, A. Roentgen examination of the inferior vena cava in retroperitoneal expanding processes. Acta radiol. 45 (1956), 289.

— — Retrograde pelvic venography. Acta radiol. 51 (1959), 401.

Kjellberg, S. R. and Olsson, S. E. Roentgenologic studies of the sphincter mechanism of the caval and pulmonary veins. Acta radiol. 41 (1954), 481.

Olivier, C. *Technique de la radiographie de la veine cave inférieure.* Mém. Acad. Chir. 77 (1951), 324.

O'Loughlin, B. J. Roentgen visualization of the inferior vena cava. Amer. J. Roentgenol. 58 (1947), 617.

Viallet, P., Chevrot, L., Aubry, P. et coll. *Compression cave inférieure dans les hépato-splénomégalies.* J. Radiol. Electrol. 38 (1957), 271.

Winkler, K., Tygstrup, N. and Hansen, A. T. Increased abdominothoracic venous pressure gradients in patients with cirrhosis of the liver. Gastroenterology 38 (1960), 914.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR ULF RUDHE) CHILDREN'S HOSPITAL, KAROLINSKA SJUKHUSET STOCKHOLM, SWEDEN

PARTIAL PERSISTENCE OF THE DUCTUS ARTERIOSUS

by

CARLOS QUIROGA

A small dimple in the endothelium of the pulmonary trunk at its division into right and left branches is frequently found in cardiovascular specimens and marks the attachment of the obliterated ligamentum arteriosum A persistent patency of the ductus represents an aberration of the obliterating process normally taking place in the postnatal period A partial persistence of the ductus lumen with patency of its pulmonary end but with the aortic end obliterated is considered rare GREIG et coll (1954), have observed such patency in only one out of 148 adult cadavers in which the ductus area was examined The case mentioned by KJELLBERG et coll (1959) appears to be the only one in which this was demonstrated by angiocardiography

It is the purpose of the present work to give an account of the frequency of this condition and its angiocardiographic appearances in a series of congenital heart lesions

Twenty five instances of a partially open ductus arteriosus were found in the angiocardiograms of 735 cases in which the pulmonary artery was contrast filled in various congenital heart lesions These figures correspond to an incidence of 3 45 %

The distribution is shown in the Table This demonstrates that the occurrence of a partially patent ductus was mainly associated with malformations causing some kind of obstruction to the outflow of the right ventricle Thus pulmonary valvular or infundibular stenosis mostly in combination with a ventricular

Submitted for publication 3 August 1960

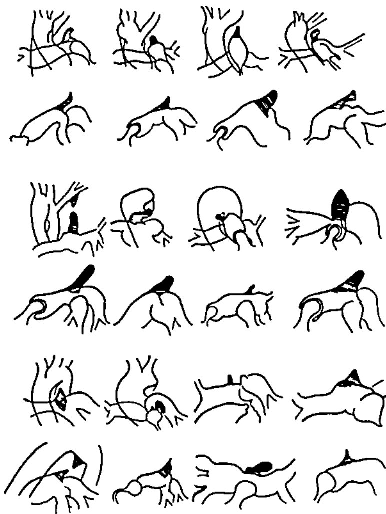


Fig 1 Schematic drawings Frontal and lateral representations of main angiocardiographic features of the great vessels in a selection of 13 cases with partially patent ductus arteriosus

septal defect, was present in 22 of the 25 cases, in approximately half of the cases the existence of a right sided aortic arch was noted A reduction of the pulmonary vascularity was observed in 21 cases A left to right shunt or a bidirectional shunt occurred in 19 cases, and 2 cases had a left to right shunt

The various shapes of the ductus remnant and its relationships to adjacent vascular structures are demonstrated by the drawings in Fig 1 As is evident from this figure, and from Figs 3 and 4, the patency of the ductus was confined to its pulmonary termination, and in no single case in the series reviewed to its aortic end The ductus emerged from the superior and dorsal part of the pulmonary artery at the origin of the left main branch, only in one case did it communicate with the right pulmonary artery The mouth of the ductus invariably was widely open and the patent portion of the ductus was as a rule

Table

Occurrence of partially patent ductus arteriosus in 25 cases of congenital heart lesions

	Number of cases	Right sided aortic arch	Left sided aortic arch	Associated anomalies: V.S.D.	Associated anomalies: A.S.D.	Associated anomalies: Stenosis of pulm. branches	Shunt: Right-to-left	Shunt: Left-to-right	No shunt	Pulmonary circulation: Decreased	Pulmonary circulation: Normal
Pulmonary stenosis in fundibular and/or valvular	22	13	9	19	2	1	19	2	1	19	3
Transposition of great vessels	2		2	1+2 vps						2	
Coarctation of the aorta	1		1						1		1
Total	25	13	12	21	2	1	19	2	2	21	4

vps = valvular pulmonary stenosis
V.S.D. = ventricular septal defect
A.S.D. = atrial septal defect

longest in cases with a right sided aortic arch. The arrangement of the vascular structures in one case suggested that the ligamentous portion of the ductus was inserted into the left subclavian artery.

The ductus was identified in one case at autopsy (Fig. 5) and in two cases at operation at which it was sought. In one of these latter cases pulmonary valvotomy was performed by inserting the valvulotome through the ductus after dissecting it free from the pericardium; in the other case, the patent portion of the ductus was used for creating an anastomosis to the aorta in order to increase the blood flow to the lungs. It was observed in these three cases that the ductus in its extrapericardial portion had a ligamentous continuation that was inserted into the wall of the aortic arch.

Discussion

The present series demonstrates that a partially patent ductus can no longer be considered a rarity. The reason why such partial persistence of the ductus has apparently escaped the attention of the operator may be that the open part of the ductus may generally be expected to have an intrapericardial location and will thus not be readily detected. Our series does not offer any final indication as to the nature of the process causing the anatomic obliteration of the ductus to be confined to its pulmonary end. It can be stated only that its preponderant occurrence in conditions that are characterized by a reduced blood flow to the lungs suggests that the ductus may serve as a collateral in the



Fig 2 Girl aged 7 operated on for tetralogy of Fallot Right sided aortic arch and a partially patent ductus arteriosu a) Frontal view b) Lateral view

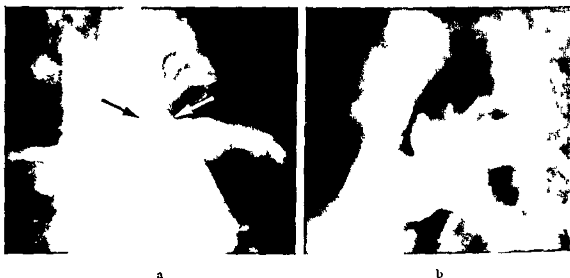


Fig 3 Boy aged 19 Infundibular and valvular pulmonary steno is ventricular septal defect right to-left hunt left ided aortic arch and a partially patent ductus arteriosus a) Frontal view b) Lateral view



Fig 4 Girl aged 3 years 6 months Ventricular septal defect infundibular stenosis right to-left shunt right sided aortic arch and a partially patent ductus arterio us a) Frontal view b) Lateral view



RPA PD LPA L PA

L PD LPA PA RPA PA

a b

Fig. 5. Autopsy specimens from infant aged 6 months. a) Tetralogy of Fallot, right sided aortic a[rch] and anomaly of the systemic arteries. The partially patent ductus measured 6 mm in length and 2 m[m] in width. The pulmonary artery is cut along its anterior wall and the ligamentous portion is retracted b[y] tweezer. Arrow points to the lumen of the ductus. b) The anterior wall of the pulmonary artery [is re]tracted upwards so that the lumen of the remnant ductus is visible. P. D. — Partially patent ductu[s]. L — Ligamental portion. P. A. — Pulmonary artery trunk, L. P. A. — Left pulmonary artery. R. P. A. — Right pulmonary artery.

postnatal period, a function that becomes interrupted by the obliteration of the ductus at its aortic termination

The widely open mouth in the pulmonary artery wall permitted the ductus easily to become contrast filled during angiocardiography The ductus invariably showed variations in size during the cardiac cycle and filled and emptied synchronously with the pulmonary artery It was never found to harbour a thrombus and was never seen to be invaded by vegetations of bacterial endocarditis In spite of the fact that in the cases combined with a right sided aortic arch the vascular structures must be expected to encircle the trachea no instance of compression of the latter was observed The partially persistent ductus should therefore be regarded as a generally innocuous abnormality That it may be a useful structure during heart operations was as mentioned above evident in two of our cases

SUMMARY

An account is given of the angiocardiographic features frequency and distribution of a partially patent ductus arteriosus in 25 cases of congenital malformations of the heart In the majority of the cases the anomaly was associated with different types of outflow obstruction of the right ventricle and in approximately half of the cases the aortic arch was right sided

ZUSAMMENFASSUNG

Das angiokardiographische Aussehen die Häufigkeit und die Verteilung eines partiell offenstehenden Ductus arteriosus in 25 Fällen mit kongenitalen Missbildungen des Herzens werden berichtet In der Mehrzahl der Fälle war die Anomalie mit verschiedenen Typen von Abflussverengungen des rechten Ventrikels verbunden und in ungefähr der Hälfte der Fälle lag der Aortenbogen rechtsseitig

RÉSUMÉ

L auteur décrit les caractères angiographiques la fréquence et la distribution de la persistance partielle du canal artériel dans 25 cas de malformations congénitales du cœur Dans la majorité des cas cette anomalie était associée à différents types d obstacles à l évacuation du ventricule droit et dans environ la moitié des cas la crosse aortique était dextroposée

REFERENCES

Greig H W Anson B J McAfee D K and Kurth L E The ductus arteriosus and its ligamentous remnant in the adult Quart Bull Northw Univ med Sch 28 (1954) 66

Kjellberg S R Mannheimer E Rudhe U and Jonsson B Diagnosis of congenital heart disease 2nd edit Year Book Publishers Chicago 1959

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An account is given of the angiocardiographic features, frequency, and distribution of a partially patent ductus arteriosus in 25 cases of congenital malformations of the heart. In the majority of the cases the anomaly was associated with different types of outflow obstruction of the right ventricle, and in approximately half of the cases the aortic arch was right sided.

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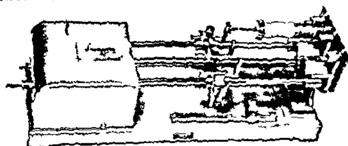
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REFERENCES

Cruice, H. W., Anson, B. J., McAfee, D. K. and Kurth, L. E.: The ductus arteriosus and its ligamentous remnant in the adult. Quart. Bull. Northw. Univ. med. Sch. 28 (1954) 66.

Kjellberg, S. R., Mannheimer, E., Rudhe, U. and Jonsson, B.: Diagnosis of congenital heart disease. 2nd edit. Year Book Publishers, Chicago 1959.



Apparatus for controlled infusions of saline and contrast media

the half nut from the screw so that the carrier can be brought into any desired position This uncoupling occurs also when the latch makes contact with an adjustable stop thus preventing syringe damage when the plunger comes near to the bottom of its travel The carrier is not pressed directly against the plunger of the syringe but the force is transmitted by means of one of the adjustable thrust rods one being used for each syringe The power from the governor controlled electric motor is transmitted to the screw by a 10 speed gear The governor permits fine adjustment between the gears, and by means of this arrangement the rate of the thrust rod can be continuously varied between 0 15 mm/min and 32 6 mm/min

We have used this machine for more than 3 years as a routine in angiography and found it to be both simple and reliable The lowest possible injection rate involving no risk of coagulation varies with the blood pressure, the elasticity of the tubing and the damping effect of the needle or catheter A lower magnitude of pulse pressure permits a lower infusion rate The greater the elasticity of the tubing the higher the injection rate must be set in order to prevent the blood from flowing into the tubing during systole and gradually clotting In a narrow and long catheter the pulse pressure is damped fairly effectively so that the infusion rate can be kept low, while when using a relatively short and wide puncture needle the infusion rate must be kept higher Under the last mentioned unfavourable conditions it has proved wise not to use an injection rate less than that corresponding to the third gear at this rate a 50 ml syringe will last for 15 minutes

The apparatus has recently been used for the injection of contrast medium in lymphography The low and constant rate of injection which is easily maintained with the apparatus gives a better filling of the deeper lymph vessels than the uneven often forced, manual injection The latter is also liable to injure the vessels

It may be mentioned that the apparatus has been successfully used for the intra arterial injection of contrast medium in laboratory animals (JEPPSON & OLIN 1960)

blood between the guide and the catheter and adhere to the former as it is withdrawn, the remainder will be washed out by the return flow of blood Physiologic saline is then infused slowly through the catheter in the usual way before and after the injection of contrast medium ÖDMAN, using a special three ribbed catheter, rinsed its lumen with heparin from time to time while the guide was still in position

Saline is thus infused sometimes for a fairly long period during angiography to minimize the risk of coagulation in the needle or catheter The rate of infusion must be low in order to avoid infusion of more fluid than is necessary Latent cerebral edema, for example in brain tumour or after head injury, may become manifest during carotid angiography if the amount of normal saline administered is excessive It is no good trying to avoid this by using Macrodex (Pharmacia) in place of saline, because in brain tumours the permeability of the capillary wall is often impaired, with the result that the dextran molecules escape into the cerebral tissue and thereby favour edema

The saline is usually infused manually with an ordinary syringe The dis advantage of this method is that it is time consuming and must be applied by a skilled operator, in addition, it is often difficult to inject at an even and low rate A flask of the type used for intravenous drip may also be used In arteriography of cases with arterial hypertension the flask must be placed 4 meter above the patient, which in practice means that the examination room must be at least 5 meter in height The tubing is also long and unwieldy We have tried this arrangement in vertebral angiography in children, with injection of the contrast medium through a catheter, but have not found it practical Another method, used by RADNER and others, for arterial catheteri zation is to infuse saline under pressure from a bottle such as used for blood transfusions The disadvantage of this method is the risk of air embolism, and accidents with this type of transfusion and infusion have occurred The method requires skilled assistants and may even then be difficult to perform in the semi darkness often necessary for catheterization

Since none of the above methods have been found very satisfactory, an automatic infusion apparatus has been adopted This is a type that has been used at the Institute of Physiology for the past 20 years for infusing various fluids into the bloodstream of experimental animals

The apparatus shown in the accompanying photograph has been con structed by one of us (B C) and consists of three main parts a syringe holder, a carrier with thrust rods, and a motor complete with gear box The holder can accommodate three syringes of 1 to 100 ml capacity which are locked in position by simple devices The carrier has two slides running on guides and driven by a long screw, the thread of which drives a half nut fastened to the lower surface of the carrier by an articulated arm This arm is spring loaded and engages by means of a latch the thread of the half nut with the thread of the screw Application of pressure against the latch will disengage

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF OLLE OLSSON) UNIVERSITY HOSPITAL, LUND SWEDEN

VERTEBRAL CATHETERIZATION VIA THE FEMORAL ARTERY

by

STEN CRONQVIST

The direct percutaneous and the catheter methods of all those proposed for vertebral angiography are the only two commonly employed We have in Lund mainly used the catheter technique introduced by RADNER in 1947 but during the last two years a technique with catheterization of the vertebral artery from the femoral artery has been tried as the primary approach in almost all cases This paper represents an analysis of our experience with this method

The technique described by RADNER involved exposure of the radial artery a small ureteric catheter being inserted through an incision in this vessel and manipulated upwards into the vertebral artery

In 1951 BIERMAN pointed out the possibility of introducing a catheter in the vertebral artery via the femoral artery LINDGREN (1956) was the first to use this route and to report clinical experiences with the method His technique consisted of percutaneous puncture of the femoral artery a catheter being introduced and inserted into the aorta and up to the aortic arch through the needle The catheter then usually slipped into the left subclavian artery and the contrast medium was injected with the tip of the catheter in the most proximal part of the vessel If the tip of the catheter could not be passed into the subclavian artery it was left in the part of the aortic arch from which the subclavian artery arises, a larger amount of contrast medium than that used when

Submitted for publication 30 August 1960

SUMMARY

An infusion apparatus for the automatic injection of physiologic saline to prevent coagulation in the needle or catheter during angiography is described The apparatus has also been used for the injection of contrast medium in lymphography as well as in angiography in laboratory animals

ZUSAMMENFASSUNG

Ein Infusionsgerät für automatische Injektion von physiologischer Kochsalzlösung um bei Angiographie eine Koagulation in der Nadel oder im Katheter zu verhindern wird beschrieben Das Gerät war auch für Injektionen von Kontrastmittel bei Lymphographie wie auch bei Angiographie von Laboratoriumstieren verwendet worden

RÉSUMÉ

Les auteurs décrivent un appareil de perfusion pour l injection automatique de sérum salé physiologique destinée à empêcher la coagulation dans l aiguille ou le cathéter au cours de l angiographie Cet appareil a aussi été utilisé pour l injection de moyen de contraste en lymphographie et en angiographie sur les animaux de laboratoire

REFERENCES

CURTIS J B Cerebral angiography Brit J Surg 38 (1950—51) 295

DAWSON H and PURVES C L An apparatus for controlled injection over long periods of time J Physiol 117 (1952) 18 P

ENGESET A Cerebral angiography with perabrodil (carotis angiography) Acta radiol (1944) Suppl No 56 p 16

JEPPSSON P G and OLIN T Cerebral angiography in the rabbit Lunds univ årsskr N F Avd 2 56 (1960) 14

LINDGREN E Röntgenologie einschliesslich Kontrastmethoden *In* Handbuch der Neurochirurgie Band II S 94 Herausgeg von Olivecrona und Tönnis Springer Berlin 1954

ÖDMAN P Percutaneous selective angiography of the coeliac artery Acta radiol (1958) Suppl No 159 p 11

RADNER S Vertebral angiography by catheterization Acta radiol (1951) Suppl No 87 p 19

SELDINGER S I Catheter replacement of the needle in percutaneous arteriography A new technique Acta radiol 39 (1953) 369

VERBRUGGHEN A Complications of iodopyracet (diodrast) arteriography Arch Neurol Psychiat 71 (1954) 518

WICKBOM I Angiography of the carotid artery Acta radiol (1948) Suppl No 72 p 90

Table

Age of patients	Number of patients examined	Catheterization Successful	Catheterization Not successful	Contrast material present in Posterior choroidal arteries	Posterior communic artery	Carotid siphon	Vertebral artery both sides
< 10	9	9	—	9	8	4	—
10—19	15	14	1	14	11	7	2
20—29	14	13	1	12	10	2	4
30—39	13	11	2	11	5	2	2
40—49	18	12	6	12	6	2	4
50—59	16	10	6	9	3	2	—
60—69	4	1	3	1	—	—	—
> 69	—	—	—	—	—	—	—
Total	89	70	19	68	43	19	12

51 patients studied in the below 40 age group Thus in this younger group successful catheterization was attained in 92 % In 2 of the cases recorded as failures the vertebral artery arose directly from the aortic arch this anomaly is stated by RADNER to occur in 6 % of cases No contrast medium to ascertain the origin of the vertebral artery was deposited in the aortic arch in the other two cases nor in the 15 failures encountered in patients over the age of 40

The vertebral angiographies successfully performed with catheterization via the femoral route were reviewed in order to evaluate the frequency of arterial spasm and to note the degree of intracranial filling of the small arterial branches

The medial and lateral choroidal arteries were chosen as criteria of a satisfactory angiogram since they are constant small have few anomalies and are of great diagnostic importance Angiograms were classified as good only when there was filling of these vessels One case was excluded from consideration because a large arterio venous aneurysm concealed these vessels

In one case spasm of the distal portion of the vertebral artery did not permit filling of its intracranial branches A slight degree of spasm was also noted in a few other cases but a filling was nevertheless obtained even of the choroidal arteries Summing up we noted filling of the posterior choroidal arteries in 68 of 69 angiographies in which catheterization of the vertebral artery had been successful This means that 98 % of these angiograms were considered as good In 43 of the 69 angiograms at least one communicating artery was filled (64 %) and in 19 cases (27 %) contrast medium could be seen in the carotid siphon

For comparison a large number of angiograms performed with direct percutaneous puncture was evaluated using the criteria previously mentioned All cases with arterio-venous aneurysm were excluded Of 176 cases the choroidal arteries were filled in 134 only 76 % of the angiograms accordingly were con

the catheterization of the subclavian artery had been successful was injected in such cases As both contrast material and a catheter in a vessel may cause spastic contractions LINDGREN avoided placing the tip of the catheter in the vertebral artery

With the newer contrast media (Hypaque, Urografin 45 %), however, we have found the degree of spasm negligible even in catheterization of comparatively small vessels such as the renal or vertebral arteries In catheterization via the femoral artery we therefore do not leave the extremity of the catheter in the subclavian artery but insert it into the proximal part of the left vertebral artery This vessel usually arises from the left subclavian artery, the two arteries together forming an almost straight line with the descending aorta, for this reason a catheter in the aorta can generally be passed directly into the vertebral artery This, at least, is the rule in young subjects but arteriosclerotic changes with deformation of the aortic arch in the elderly may make the further passage of a catheter more difficult In the latter instance a slight bend of the catheter about 2 to 3 cm from its tip often helps in the positioning

If previously we were not successful in placing the catheter in the vertebral artery we would inject a larger volume of contrast medium in either the subclavian artery or in the aortic arch We now seldom employ such a technique for vertebral angiography since the resulting roentgenograms have been found unsatisfactory

At the present time, whether catheterizing the femoral or the radial artery, we introduce the catheter in accordance with SELDINGER's technique A metal wire with a flexible tip is introduced through a needle in the artery which is then withdrawn to leave the wire in the vessel, a polythene catheter is passed over the metal wire and these together are manipulated into the selected vessel

When the catheter is to be introduced via the radial artery its entry into the vertebral artery is facilitated if a sharp bend of the catheter is made about one centimeter from the tip

In catheterization via the femoral artery the instruments necessary for the examination consist of a Seldinger needle No 205, a polythene catheter (PA 200) and a corresponding wire leader, with the radial route the number of the needle is 160 and the catheter a PA 160 A radiopaque catheter (ÖDMAN) with a small bore may also be used General anaesthesia is used only in children Vasodilating agents have as a rule not been administered The amount of contrast medium employed is 4 to 5 ml for each injection Serial films are taken in lateral and in frontal projections

We have, as stated, regularly tried this type of catheterization in almost all of our cases during the last two years Among 89 cases, we were successful in placing the catheter in the vertebral artery in 70 (78 %) It may be seen from the Table given below that the majority of failures occurred in those patients who were more than 40 years of age, we failed in 15 out of 38 examinations in which the patients were more than 40 but there were only 4 failures among

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Radner technique also apply to catheterization via the femoral artery Thus, sterile conditions and fluoroscopy are required The Seldinger instruments however will minimize the trouble caused by the necessity for a sterile field and the fluoroscopic exposure will be kept within reasonable limits by attention to the size of the diaphragm and by keeping the viewing time down to under a minute The use of an image amplifier will decrease the amount of radiation delivered both to the operator and to the patient as will the use of the TV technique This has lately been employed at Lund The latter will also minimize the risk of soiling the sterile instruments which otherwise may easily happen when working with fluoroscopy in the dark

All methods for the examination of the vertebral artery have a common disadvantage, that is, the inconstant filling of the posterior inferior cerebellar artery on the opposite side When the involved side is indicated by the clinical findings this side may readily be selected if the percutaneous puncture method is employed Routine use of the Radner technique or the Lindgren technique implies that the right or the left vertebral artery, respectively is examined It is possible to catheterize the left vertebral artery from the left arm and conversely the right vertebral artery from the femoral route This involves, however a more extensive and difficult manipulation In order to overcome this disadvantage one may attempt to fill the opposite posterior inferior cerebellar artery by injection during diastole (OLIN 1958) or by compression of the opposite vertebral artery as described by SALTZMAN The last mentioned method however as well as any other manipulations of the head may be employed to best advantage in the catheter method The use of the percutaneous route on the other hand will increase the difficulties in maintaining a correct needle position during such manipulations

Complications following vertebral angiography have not been confined to one particular technique Nevertheless a review of the literature would seem to indicate that the catheter method, as originally applied by RADNER is followed by more complications than the direct percutaneous puncture (RADNER 1951 OLSSON 1953 HAUGE 1954 SJOGREN 1953 SWANN 1958 RUGGIERO 1958 inter alios)

In the author s cases with catheterization of the vertebral artery via the femoral artery there was only one alarming cerebral complication associated with vertigo nystagmus, vomiting and a fall in blood pressure The signs were transitory however, and completely disappeared *in half an hour*

SUMMARY

The technique of catheterizat on of the vertebral artery is described Catheterization via the femoral route was found to be more successful in patients below than in patients above the age of 40 The resulting angiograms were of good quality and filling of smaller arterial branches was seen more often than in angiograms performed with direct percutaneous puncture of the vertebral artery

sidered as 'good'. Most of the examinations were made, however, before the apparatus for rapid serial angiography was in use.

Rapid serial angiography was employed in all the examinations performed with catheterization via the femoral artery. In a review of the angiographic filling of the posterior communicating and posterior cerebral arteries, SALTZMAN noticed no significant difference in the degree of filling of these vessels when 'conventional' studies were compared with rapid serial angiograms. Thus the results obtained with the two different types of examination — catheterization on the one hand and direct percutaneous puncture on the other — may reasonably be compared.

Various investigators have published their experiences with the percutaneous puncture technique. LINDGREN (1950) reported filling of the arteries in the posterior fossa in two thirds of cases in or above middle age. SJOGREN in a material of more than 150 cases succeeded in puncturing the vertebral artery in all but 2 cases, in 10 cases the filling of the intracranial branches of the vertebral artery was not satisfactory. The major problem in percutaneous puncture, as pointed out by SJOGREN, is to maintain the tip of the needle in the correct position within the vessel. Various needles have been designed to facilitate this (SJOGREN 1953, SHELDON 1956, SWANN 1958). SWANN (1958) reported successful examinations in 94 % of the cases in which a modified Sheldon needle was employed, SWANN's earlier experiences with conventional needles were not satisfactory, success being attained in only 60 % of cases examined. RUGGIERO et coll. (1958) succeeded with percutaneous puncture in 225 out of 227 examinations (99.1 %), 33 of the examinations were not satisfactory enough to permit a definite diagnosis. This means that in 194 cases or 85.5 % the authors considered the resulting angiograms acceptable.

RADNER and HAUGE reported successful catheterization with the Radner technique in 98 and 98.5 % of cases, respectively. In 1953, OLSSON added another 140 cases to those already published by RADNER. In this series right-sided catheterization failed in 3 cases but the examination was completed by catheterizing the left side, in one case the examination was interrupted by arterial spasm. BONTE, RIFF & SPY (1958) described the results in 75 angiographies in patients ranging from 6 to 70 years of age. These investigators used the catheter technique as described by LINDGREN. In their series it was possible to place the tip of the catheter in the left vertebral artery in 23 cases and in the right vertebral artery in one case, in 19 cases it lay in the first part of the subclavian artery and in 2 cases in the aortic arch at the origin of the left subclavian artery. These authors considered the examination to have been successful in 45 cases or 60 %.

The two catheter methods, as well as the puncture technique have advantages as well as disadvantages. Percutaneous puncture of the vertebral artery may be a painful experience to the patient, while a puncture of the radial or femoral artery is readily tolerated. Some of the arguments raised against the

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LOCALIZATION WITH Sr^{8} OF SPINAL METASTASES IN MAMMARY CANCER AND CHANGES IN UPTAKE AFTER HORMONE AND ROENTGEN THERAPY

A preliminary report

by

INGE GYNNING, PER LANGELAND, STURE LINDBERG and BERNDT WALDESKOG

Skeletal metastases are often not demonstrable in the roentgenogram until bone destruction is considerable. This applies particularly to the spine. A comparison between roentgen and postmortem findings as well as experimental studies by BABAIANTZ, have shown that the bone decalcification must reach about 50 % before it is evident in the roentgen film.

Investigations with so called osseophil isotopes in recent decades have contributed considerably to our knowledge of the mineral metabolism of the skeleton. Such isotopes have also been used in the elaboration of methods enabling an earlier diagnosis of osseous tumours. The distribution of radio gallium (Ga^{66}, Ga^{67} and Ga^{72}) in the skeleton and their concentration in *osseous lesions, particularly tumours, have been studied by* DUDLEY et coll. (1950, 1956), DESGREZ (1954), DESGREZ et coll. (1954) and MULRY et coll. They have shown that occasionally an accumulation of radiogallium may be demonstrated in osseous tumours before it can be detected at roentgen examination.

The method has been used in examinations for primary osseous tumours as well as skeletal metastases. DESGREZ et coll. claim to have shown that a tumour is sometimes more extensive than may be assumed from its roentgenographic appearance, an observation of importance in the radiotherapy

Submitted for publication 25 August 1960

ZUSAMMENFASSUNG

Die Technik der Katheterisierung der A. vertebralis wird beschrieben. Die Katheterisierung auf dem femoralen Wege war bei Patienten im Alter von unter 40 Jahren erfolgreicher als bei denen, die älter waren. Die so erzielten Angiogramme waren von guter Qualität und die Füllung kleiner Arterienäste wurde hier öfter als in den Angiogrammen beobachtet, die nach direkter perkutaner Punktion der A. vertebralis hergestellt wurden.

RÉSUMÉ

L'auteur décrit la technique du cathétérisme de l'artère vertébrale. Le cathétérisme par voie fémorale est plus souvent couronné de succès avant qu'après l'âge de 40 ans. Il donne des angiographies de bonne qualité et opacifie plus souvent les fins rameaux artériels que les angiographies exécutées par ponction percutanée directe de l'artère vertébrale.

REFERENCES

Bierman, H. R., Miller, E. R., Byron, R. L., et coll.: Intra arterial catheterization of viscera in man. Amer. J. Roentgenol. 66 (1951), 555.

Bonte, G., Riff, G. et Six, J.: Angiographie vertébrale par cathétérisme rétrograde fémoral. Acta radiol. 50 (1958), 67.

Galloway, J. and Greitz, T.: The medial and lateral choroid arteries. An anatomic and roentgenographic study. Acta radiol. 53 (1960), 353.

Hauge, T.: Catheter vertebral angiography. Acta radiol. (1954) Suppl. No. 109.

Krayenbühl, H. und Yasargil, M. G.: Die vaskulären Erkrankungen im Gebiet der Arteria vertebralis und Arteria basilaris. Georg Thieme, Stuttgart 1957.

Lindgren, E.: Percutaneous angiography of the vertebral artery. Acta radiol. 33 (1950), 389.

— Handbuch der Neurochirurgie Bd. II. Springer Verlag, Heidelberg 1954.

— Another method of vertebral angiography. Acta radiol. 46 (1956), 257.

Löfgren, F. O.: Vertebral angiography in the diagnosis of tumours in the pineal region. Acta radiol. 50 (1958), 108.

Olin, T.: EKG-styrd kontrastinjektion vid angiografi (Swedish). 22nd Congr. Nord. Foren. med. Radiol. Åbo 1958.

Olsson, O.: Vertebral angiography. Acta radiol. 40 (1953), 103.

Radner, S.: Intracranial angiography via the vertebral artery. Acta radiol. 28 (1947), 838.

— Vertebral angiography by catheterization. Acta radiol. (1951) Suppl. No. 87.

Ruggiero, G., Thibault, A. et Bories, J.: L'artériographie vertébrale dans le diagnostic neuro-chirurgical. Acta radiol. 50 (1958), 365.

Saltzman, G. F.: Angiographic demonstration of the posterior communicating and posterior cerebral arteries. Acta radiol. 52 (1959), 1.

— Circulation through the posterior communicating artery in different compression tests. Acta radiol. 51 (1959), 10.

Sheldon, P. A. W.: A special needle for percutaneous vertebral angiography. Brit. J. Radiol. 29 (1956), 231.

Sjögren, S. E.: Percutaneous vertebral angiography. Acta radiol. 40 (1953), 113.

Swann, G. F.: Vertebral arteriography using the Sheldon needle and modification of it. Brit. J. Radiol. 31 (1958), 23.

Takahashi, K.: Die perkutane Arteriographie der Arteria vertebralis und ihrer Versorgungsgebiete. Arch. J. Psychiat. 111 (1940), 373.

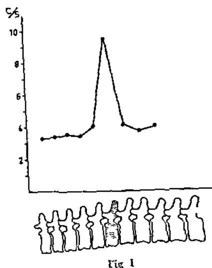


Fig 1

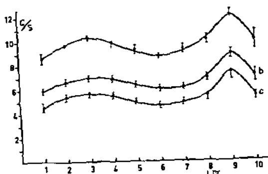


Fig 2

Fig 1 Curve illustrating a high counting rate over a vertebra with metastases 7 days after injection

Fig 2 Normal curve for activity over spine Counting rates determined over 10 levels of the spine a) 1 week b) 2 weeks and c) 3 weeks after injection of 50 μC Sr[8]

metastases if present could be readily detected by variation in the quotient between the values obtained over the two knees These measuring points are easy to identify The outer aperture of the collimator was placed directly against the skin and the time for 1 000 counts was noted Two determinations were made over each measuring point with reposition of the detector Each patient was studied one, two and three weeks after the injection When the roentgen examination suggested pelvic metastases measurements were made over the suspected area as well as over the corresponding contralateral area

A repeat series of measurements were performed usually at an interval of about 6 months The activity over the spine and the knees was also measured before the injection of the isotope for such repeat studies These basic values were subtracted from the measuring values found after the repeated injection The detector was placed over the same measuring points as on the previous occasion with the aid of roentgenograms with markers

For judging to what extent an accumulation of Sr^{85} in metastases might be expected a number of patients with known skeletal metastases were studied All the patients showed a marked accumulation of the isotope in the region with roentgen changes (Fig 1)

Examinations were later made of a number of patients with tumour but without probable skeletal metastases This preliminary examination of 7 selected patients with a roentgenologically normal spine apart from insignificant osteitis deformans changes showed the differences in the counting rate over corresponding points to be surprisingly small Mean values of the counting rate over the 10 measuring points in these 7 cases were therefore calculated

of the lesion According to DESGREZ et coll and DUDLEY et coll (1956) ir radiation can depress the readiness with which a tumour takes up radiogallium

Recent investigations have revealed that strontium has a more specific affinity for bone than gallium and must therefore be preferred in examinations for osseous tumours The first to use radiostrontium clinically were TREADWELL et coll, who as early as 1942 showed that Sr^{89} accumulates in neoplastic osseous tissue Their observation has since been confirmed by BAUER for example, who used Sr^{85} BAUER et coll (1957, 1958, 1959, and work not yet published) have studied osseous metabolism not only by urine analysis and measurement of the radioactivity of the blood but also by external measurements for which they used mainly Sr^{85} and Ca^{47} They studied tumours as well as a number of other osseous conditions and gave information of clinical value regarding the diseases in which an increased uptake may be expected

The investigations referred to above prompted us to study the uptake of Sr^{85} by the spine in patients operated upon for cancer of the breast The purpose of the investigation was to assess the value of the isotope for making an early diagnosis of spinal metastases, for charting the spread of the tumour, and for comparing the uptake of the isotope by the lesions before and after different types of treatment (local roentgen irradiation and hormone treatment) In order to permit a comparison between the value of the isotope technique and the roentgen examination in the early diagnosis of osseous tumours of the spine, roentgenograms were taken every time the isotope was injected

Sr^{85} is a pure gamma ray emitter with an energy of 0 51 MeV, its half life is 65 days For each examination the patient received 50 μC Sr^{85} intravenously

Measurements were made with an LKCO scintillation detector mounted in an LKB collimator The latter can be provided with different cones, and in the present investigation a cone with a 12° opening angle and a diameter of 65 mm was used Pulses from the photomultiplier were amplified in an EKCO linear amplifier and then fed into a Tracerlab superscaler via a single channel pulse analyzer The 'window used was placed over the gamma peak The apparatus was the same as that used by BAUER et coll (1959) The stability of the apparatus was continuously checked For this purpose Na^{22} was used as well as a stock solution of Sr^{85} All of the measurements were normalized against the counting rate of the stock solution This was determined before and after measurement on the patient, and a mean value was used for the normalization

Measuring technique Measurements were made at 10 levels of the spine, spaced 6 cm apart This distance was selected because the collimator cone with an opening of 65 mm diameter covered about 10 cm of the spine Measurements were also made as a routine bilaterally over a point situated centrally at the upper border of the patella This was done to obtain values for a part of the skeleton which was probably not involved by metastases and in which

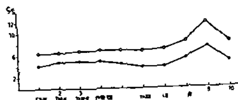


Fig 3 Measurements at 6 month intervals The second curve is higher but of same shape as the first one ● August 21st 1958 ○ February 4th 1959



Fig 4 Measurements at 6-month intervals with no manifest changes in the general condition or in the roentgen findings Good agreement between the curves ● September 18th 1958 ○ March 10th 1959 △ September 10th 1959

to the highest value for the factor *f* which is the quotient between the measured value and the corresponding normal value

It is clear from the table that in the majority of the cases in group I the highest factor was below 1 5, while none of the cases in group II lay in this subgroup In sharp contrast a factor of more than 2 was found in only 2 cases in group I against 24 in group II

No spinal metastases or fractures were roentgenologically demonstrable in group I One of the patients belonging to group II B had metastases while 14 patients in group II C had spinal metastases and 3 had compression fractures No explanation can be offered for the abnormal measuring values or the configuration of the spine curve in those cases in which roentgen examination had shown no signs of a pathologic condition Repeated Sr^{85} tests and roentgen examination at relatively short intervals as well as autopsy findings may with time provide an explanation for the variation in the order of magnitude of the factor *f* and of the configuration of the curve All that can be said for the time being is that any appreciable deviation from the normal configuration of the curve suggests metastases

The long term investigation of cancer of the breast stage II 3, which is in progress with regular examination of the distribution of Sr^{85} at 6 monthly intervals and comparison with the roentgen findings has already yielded useful information It has been found *for example* that *advanced osteitis* deformans may give high values and as demonstrated previously by BAUER et



Fig 5 Case of mammary carcinoma stage II group 3 Primary normal spine activity curve Increasing values with maximum in the lower lumbar region indicating metastases Roentgen examination negative ● March 18th 1959 ○ September 16th 1959 △ March 19th 1960

Table

Group	A $0.9 \leq f < 1.5$	B $1.5 \leq f < 2.0$	C $f \geq 2.0$	Number of cases	Metastases fractures shown by roentgen
I Normal shape of spine activity curve	27	9	2	38	0
II Abnormal shape of spine activity curve	0	8	24	32	18

and plotted as a function of the measuring points (Fig 2) The curves are based on measurements made one, two and three weeks after the injection of strontium The curves showed one peak over the middle thoracic spine and another over the sacro lumbar region The shape of the curve is due mainly to the volume of the skeleton covered by the detector and to variations in the distance between the skeleton and the detector owing to the curvature of the spine The curve obtained for the spine is hereinafter referred to as the 'normal curve' No appreciable difference was found in any of these seven cases between the values noted over the two knees

A question often requiring consideration in the planning of treatment of a large group of patients with cancer of the breast is whether there is any suggestion of skeletal metastases A total material of 70 cases of cancer of the breast were therefore selected for clinical trial, almost half of them (30 cases) immediately after the operation The latter belonged to stage II group 3 according to NOHRMAN's nomenclature and had thus had metastases in the axillary lymph nodes with a periglandular spread It is known that 75 % of such patients must be expected to die within 5 years, within this period this group will therefore probably include a relatively large number of cases with skeletal metastases Examination with Sr^{8} was repeated at intervals of about 6 months The purpose of this long term investigation was to ascertain whether by this method skeletal metastases could be detected earlier than in the roentgen examination In some cases this appeared to be possible

The rest of the series (40 cases) consisted of cases of cancer of the breast with roentgenologically demonstrated or clinically suspected skeletal metastases

After the curves had been compared with the normal curve the material was first divided into two groups according to the measurements made over the spine Cases with a spine curve of normal configuration, irrespective of the level of the curves, were assigned to the first group and those with an abnormal configuration to the second group

Of the whole material of 70 cases 38 belonged to group I and 32 to group II, as may be seen from the Table above A detailed analysis of these cases is in progress

These two groups were divided into three subgroups A, B and C, according

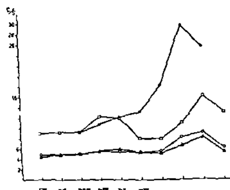


Fig 7 Measurements in a case with widespread metastases Irradiation of lumbar spine in February—March 1958 Androgenic hormone therapy Resemblance with lowest curve in fig ? Clinical improvement Hypercalcaemia in middle of 1959 Androgenic hormone therapy replaced by cortisone Deterioration ● March 27th 1958 ○ November 5th 1958 △ May 13th 1959 □ December 1st 1959

spinal secondaries Metastases however were found in L 4 on further roentgen examination 2 months later It is thus evident that Sr^{85} can detect skeletal metastases before they give rise to symptoms and it would therefore appear that the method is a useful supplement to the routine roentgen examination

The isotope technique was also studied for its capacity to reveal the effect of palliative treatment of cases with widespread skeletal metastases For this purpose patients were selected in whom a series of Sr^{85} measurements had been made on three or four occasions after irradiation or institution of hormone therapy The first test was performed at the beginning of treatment The examinations are of particular interest with respect to those changes that can be recorded in the isotope uptake and correlated with the clinical course after therapy has been started

Case reports

Case 1 A woman aged 54 operated upon in 1947 for cancer of the breast stage I who when returning 11 years later complained of pain in the lower thoracic spine Roentgen examination revealed widespread metastases in the ribs spine and pelvis In October 1958 Sr^{85} showed increased values over all measuring points of the spine and an irregular curve (Fig 6a) The patient was given androgenic hormone therapy A month later she was submitted to bilateral oophorectomy after which she received roentgen irradiation of the lower thoracic spine and later of the lumbar spine In April 1959 a general further increase of the Sr^{85} values was noted within the area irradiated four months previously the increase was however relatively smaller The patient felt worse with increasing pain and further roentgen examination showed progression of the metastases The relatively smaller *increase in the counting rate over the irradiated area was noteworthy and was ascribed mainly to the irradiation in accordance with previous investigations with radiogallium In an attempt to elucidate this the quotients between the counting rates over the corresponding points were plotted as a function of the 10 measuring points (Fig 6b) The quotients were normalized to point 5 (Th 3 The figure clearly shows the difference in the counting rate between the non irradiated and irradiated areas

New measurements were made after androgenic hormone therapy had been replaced by

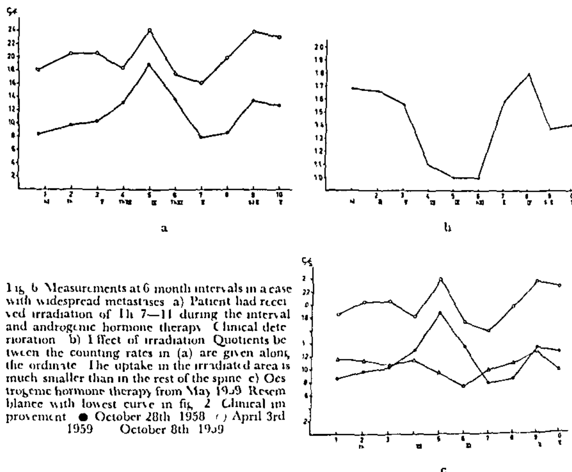


Fig. 6. Measurements at 6 month intervals in a case with widespread metastases. a) Patient had received irradiation of Th 7—11 during the interval and androgenic hormone therapy. Clinical deterioration. b) Effect of irradiation. Quotients between the counting rates in (a) are given along the ordinate. The uptake in the irradiated area is much smaller than in the rest of the spine. c) Oestrogenic hormone therapy from May 1959. Resemblance with lowest curve in fig. 2. Clinical improvement. ● October 28th 1958. ○ April 3rd 1959. October 8th 1959.

coll (1959) that fractures produce markedly high values. In some cases the level of the curve varied slightly in the absence of any manifest change in the general condition of the patient (Fig. 3). As will later be apparent external factors such as endocrine balance may be of significance. In some cases good agreement was found between the values noted on different occasions (Fig. 4).

It was as mentioned considered of interest to ascertain whether it is possible to demonstrate changes earlier by means of Sr^{85} than by roentgen examination. Slight changes in the roentgenogram were often not detected until re-examination after Sr^{85} had in fact suggested the possibility of these being present. In some cases, however, no agreement was found between the two methods (Fig. 5). The shape of the spine curve was normal at the time of the initial measurement, with a highest factor of 1.6. On re-examination half a year later the values found for the lower spine had increased with a maximal factor of 1.8 and at the final measurement, 1 year after operation, the values had increased further, with a considerable change in the shape of the curve 1 and a maximal factor of 3.2 over the fourth lumbar vertebra and of 2.9 over the second sacral vertebra. The patient felt well and roentgen examination showed no signs of

SUMMARY

An isotope technique with Sr^{85} for detecting metastases in mammary carcinoma by external measurement of the radioactivity over the spine is described with reference to a material of 70 cases The method is a good complementary method in the routine examination of patients with cancer of the breast and will sometimes demonstrate metastases earlier than roentgen examination Changes in the isotope uptake in association with palliative irradiation and hormone therapy are exemplified

ZUSAMMENFASSUNG

Eine Isotoptechnik mit Sr^{85} zur Entdeckung von Metastasen bei Mammakarzinomen mit Hilfe externer Messungen der Radioaktivitat uber der Wirbelsaule wird unter Bezugnahme auf ein Material von 70 Fallen beschrieben Die Methode ist ein gutes Komplement bei der ublichen Untersuchung von Patienten mit Brustkrebs und erlaubt es gelegentlich Metastasen fruhzeitiger zu demonstrieren als es mit Hilfe der Rontgenuntersuchung moglich ist Veranderungen der Isotopenaufnahme bei gleichzeitiger palliativer Bestrahlung und Hormontherapie werden mit Beispielen belegt

RÉSUMÉ

Les auteurs décrivent sur un matériel de 70 cas une technique isotopique avec Sr^{85} pour detecter les métastases du cancer du sein par la mesure externe de la radioactivité au dessus de la colonne vertébrale Cette méthode est un bon complément de l examen standard des malades atteintes de cancer du sein et mettra parfois en évidence des métastases plus precocement que l examen radiologique Les auteurs donnent des exemples de modification de la fixation de l isotop sous l effet de la radiothérapie palliative et de l hormonothérapie

REFERENCES

BABAIANTZ I Les osteopathies arthrophiques J Radiol Électrol 29 (1948) 333

BAUER G C H *Skeletal metabolism in humans studied with body surface counting of* Sr^{85} and Ca^{47} UNESCO Int Conf Radioisotopes Paris 1957 Vol 4 p 232 Edited by R C *Extermann Pergamon Press London 1958*

— and RAY R D Kinetics of strontium metabolism in man J Bone Jt Surg 40 A (1958) 171

— and WENDEBERG B External counting of Ca^{47} and Sr^{85} in studies of localized skeletal *lesions in man J Bone Jt Surg 41 B (1959) 558*

DESGREZ M H La detection des traceurs radioactifs émetteurs a l aide de collimateurs à *faible ouverture Bull* Acad nat Med 138 (1954) 474

— GUERIN R A et GUERIN M T Le test au 72 gallium dans les tumeurs malignes des os *Presse med 62 (1954) 397*

DUDLEY H C IMIRIE G W and ISTOCK J T Deposition of radiogallium (Ga^{72}) in pro*liferating tissues* Radiology 55 (1950) 571

— MADDOX G E and LA RUE H C. Studies of the metabolism of gallium J Pharmacol *exp Ther 96 (1949)* 135

— MARKOWITZ H A and MITCHELL, T G Studies of the localization of radioactive *gallium (Ga^{72}) in* bone lesions J Bone Jt Surg 38 A (1956) 627

JOWSEY J RAYNER B TUTT M and VAUGHAN J The deposition of Sr^{90} in rabbit bones *following intravenous injection* Brit J exp Path 34 (1953) 384

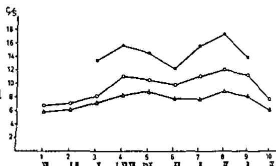


Fig 8 Measurements in a case with widespread metastases Androgenic hormone therapy Resemblance with lowest curve in fig 2 Clinical improvement ● *March 1st 1958* ○ *August 19th 1958* △ *February 14th 1959*

oestrogenic hormone therapy a month later The patient had improved and at the time of this measurement a fall was noted in the values recorded over all points (Fig 6c)

Case 2 A woman aged 57 operated upon for cancer of the breast stage I in 1949 who returned 9 years later complaining of skeletal pain On roentgen examination widespread metastases of the spine and pelvis were found In February 1958 she had received irradiation of the lumbar spine and was afterwards submitted to bilateral oophorectomy followed by androgenic hormone therapy The first Sr^{85} test was performed a month later Measurement showed generally increased values over the entire spine with a maximum over the lumbar region (Fig 7) Following treatment the patient was free from symptoms and at two subsequent examinations with Sr^{85} the spine curve was found to be almost normal This was interpreted also as an effect of therapy Roentgen examination showed an improvement in the calcium content of the affected bones and a recovery of skeletal structure

Hypercalcaemia secondary to treatment with androgenic hormone occurred just over a year later and the treatment had to be withdrawn This was followed by pain in the lower thoracic spine Re examination with Sr^{85} showed that the values had again begun to rise and were highest over the region of the pain The patient has since been treated with androgenic hormone combined with cortisone the pain has disappeared her general condition has improved and she is able to carry on with her usual work

Case 3 A woman aged 49 with inoperable ulcerative cancer of the breast was treated with roentgen irradiation and afterwards by mastectomy Roentgen examination showed a left pleural effusion and skeletal metastases The patient was treated with radioactive gold to the pleura and bilateral oophorectomy followed by androgenic hormone therapy The pain disappeared and the patient felt better No roentgen treatment was given The Sr^{85} curve plotted at the beginning of the hormone therapy was abnormal (Fig 8) Also in this case the shape and level of the curve on two later occasions tended to return to normal on clinical improvement of the patient

In those cases in which hormone therapy produced clinical improvement the values and the shape of the Sr^{85} curve tended to return to normal, while clinical deterioration was accompanied by a rise in the Sr^{85} values

The observations set forth above are based on preliminary examinations They will be supplemented by detailed analyses of the excretion of strontium in the urine of cases with skeletal metastases and in normal controls In this long term study an analysis of the blood, urine, and faeces in special cases will also receive due attention A scintillographic technique for examining selected parts of the skeleton is being devised

FROM THE SURGICAL ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR ROLF KOHLER) UNIVERSITY CENTRAL HOSPITAL HELSINKI FINLAND

CLEANSING OF THE LARGE BOWEL BEFORE ROENTGENOLOGIC EXAMINATION OF THE ABDOMEN

by

ROLF KOHLER and ESKO TAHTI

An essential condition for the achievement of a good result in the roentgen examination of the abdomen is a satisfactory preparation of the large bowel

The object of the present work was to find out which of three methods of evacuation cleanses the colon most effectively to discover which method is the least time consuming for the nursing staff and the patient seems to prefer to find out whether the patient s age has any effect on the efficacy of the preparation and to establish whether and to what extent prolongation of the interval between the last cleansing measure and the roentgen examination affects the distribution of gas in the stomach small intestine and colon

Methods and Material

The cleansing methods were as follows

A The day before the examination the patient was kept on a light diet and at 10 a m given 15 ml castor oil per os and in the evening in the ward an enema of 1 5 l water the latter being repeated on the morning of the examination

B A light diet the day before the examination and at 10 a m 15 ml castor oil per os On the morning of the examination an enema of 1 5 l water was

Submitted for publication 29 June 1960

KIDMAN B, RAYNER, B, TUTT, M and VAUGHAN, J Autoradiographic studies of the deposition of Sr^{89} in rabbit bones J Path Bact 64 (1952) 453
MULRY, W C and DUDLEY H C Studies of radiogallium as a diagnostic agent in bone tumours J Lab clin Med 37 (1951), 239
NOHRMAN, B A Cancer of the breast Acta radiol (1949) Suppl No 77
RUFFO A MARINONI, U, SIGNORELLI, L et coll La fissazione dello stronzio radioattivo (^{124}Sr) nel sistema scheletrico dopo surrenectomia bilaterale e ipofisectomia Minerva Chir 12 (1957), 876
SPENCER H BROTHERS, M, BERGER E et coll Strontium 85 metabolism in man and effect of calcium on strontium excretion Proc Soc exp Biol 91 (1956) 155
DE TREADWELL, A, LOW BEER B V A FRIEDELL, H L and LAWRENCE J H Metabolic studies on neoplasma of bone with the aid of radioactive strontium Amer J med Sci 204 (1942) 521
VAN DER WERFF J TH Clinical investigations on the use of radioactive gallium (Ga^{66} and Ga^{67}) in bone diseases Acta radiol 41 (1954) 343

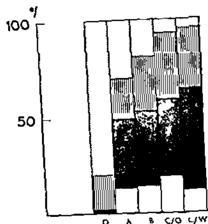


Diagram showing the results of assessment of the volume of gas and the colonic contents in control patients and patients evacuated with the aid of methods A, B and C. The percentual distribution into four groups is according to the classification given in the text. O = control patients. C/O = method C on outpatients. C/W = method C on ward patients. White sections indicate excellent, black sections good, striped sections fair and dotted sections poor evacuation.

castor oil and Clysodrast in just under one fifth of the cases. It is worthy of note that 2 % of the unprepared patients ranged into group II and 16 % into group III.

As already mentioned, the enema was given in the wards. This is probably the principal reason why the result in the group treated according to method A was unexpectedly poor. An enema is effective only if administered by specially trained personnel and can be done best in the roentgen department. This view was expressed by WELIN (1958) whose results with Clysodrast Novum enemas given in the roentgen department were excellent and constituted a firm foundation for the successful application of the double contrast method in examinations of the large bowel.

Technical nursing aspects of colonic evacuation. Cleansing of the bowel by means of tablets and suppositories requires only a minimal expenditure of time by the nursing staff and in this respect is far superior to the enema. Of the irrigation methods, Clysodrast is the slowest, as the patient often experiences abdominal pain, though this passes over if there is a short pause in the filling of the bowel. Metalax has been greeted with satisfaction by the staff in the heavily over-worked and cramped conditions of the outpatient department. The large accumulation of morning enemas has been reduced by the home preparation for the roentgen examination. Of the 120 ambulant cases questioned, 78 % professed to prefer Metalax purgation to an enema, principally because the former causes less discomfort.

The laxative effect of Metalax tablets usually began in 8 to 12 hours, the stools being mostly of a loose consistency. The tablets proved ineffective in 8 % of the cases; when this happened, the bowel was emptied with the aid of a Metalax suppository, which failed to produce an effect in only 5 cases. In two thirds of the cases the suppository had a latent period of 15 min and

given with one container of Clysodrast Novum (Ferrosan, Malmo, Sweden), a preparation consisting of 4 4 diacetoxydiphenyl pyridil (2) methane and tannin

C A light diet the day before the examination and at 7 p m 3 tablets of Metalax 0 005 g (Star, Tampere, Finland, to whom we are indebted for the tablets as well as the suppositories) The evacuating component is identical with that in Clysodrast and is contact laxative which affects only the large bowel On the morning of the examination the patient received 1 Metalax suppository 0 01 g an hour before the beginning of the examination In investigations of the colon the evacuation was commenced the day before at 3 p m with 1 Metalax suppository For the pharmacologic and physiologic effects of the substance reference is made to EKLOF (1958) who used Dulcolax (C H Boehringer & Sohn, Ingelheim am Rhein, Western Germany) of the same composition as Metalax

The cleansing results in 567 patients were compared, 240 were to undergo urography, 191 cholecystography and 136 an examination of the colon The material also included as controls 100 outpatients who had not been prepared 115 ward patients were prepared by the method A with a cleansing enema, and 105 by method B with Clysodrast, 138 outpatients and 209 ward patients were prepared by method C with Metalax

An ordinary film of the abdomen was obtained half an hour to three quarters of an hour after the last evacuation The volume of gas in the stomach, small intestine and colon and the volume of the colonic contents were classified as follows (I) excellent = insignificant amounts of gas in the alimentary tract, (II) good = only small amounts of gas in the alimentary tract or a very scanty colonic content, (III) fair = moderate amounts of gas or colonic contents, enough to interfere with the diagnostic evaluation of the films, (IV) poor = much gas or large residues in the alimentary tract, making it impossible to perform a satisfactory evaluation

A further routine film was taken in 174 cases one hour after the first to determine how the longer interval between the evacuation and examination affected the volume of gas in the organs concerned

Results

Colonic evacuation The distribution of the results in the control material and after evacuation according to methods A B, and C are shown in the Diagram, p 131 The cases treated according to method C have been divided into an outpatient and a ward patient group As may be seen from the diagram, the evacuation following Metalax was the most complete, with little difference between outpatients and inpatients, in nearly one third of the cases, castor oil and an enema gave a poor result, and the same was true of

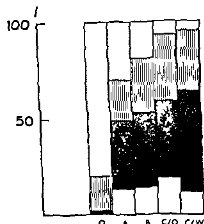


Diagram showing the results of assessment of the volume of gas and the colonic contents in control patients and patients evacuated with the aid of methods A B and C The percentual distribution into four groups is according to the classification given in the text O = control patients C/O = method C on outpatients C/W = method C on ward patients White sections indicate excellent black sections good striped sections fair and dotted sections poor evacuation

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SUMMARY

A comparative study was made in 567 cases of the results of preparation of the colon by castor oil and a water enema castor oil and Clysodrast Novum enema and tablets and suppositories containing the same contact laxative as Clysodrast viz dioxyphenylisatin The most effective evacuation of the colon was produced by the last method

ZUSAMMENFASSUNG

In 567 Fällen wurde eine vergleichende Studie über die Resultate der Vorbereitung des Dickdarmes mit folgenden Medikationen unternommen purgativem Öl und Wassereinlauf Öl und Clysodrast Novum Einlauf und Tabletten und Suppositorien die dasselbe Kontaktlaxans wie Clysodrast i e Dioxyphenylisatin enthalten Die wirksamste Entleerung des Dickdarmes wurde mit der letztgenannten Methode erzielt

RÉSUMÉ

Les auteurs ont comparé sur 567 cas les résultats de la préparation du colon par l huile de ricin et un lavement d eau l huile de ricin et un lavement au Clysodrast Novum et des comprimés et des suppositoires contenant le même laxatif de contact que le Clysodrast c est-à-dire la dioxyphenylisatine C est cette dernière méthode qui donnait la meilleure évacuation du colon

REFERENCES

EKLOF O Dulcolax ett kontaktlaxativ och dess användning inom rontgenologin (Swedish) Nord Med 60 (1958) 1566

MIES J Erfahrungen mit einem Kontaktlaxans unter besonderer Berucksichtigung als Vorbereitungsmittel zur Rontgenuntersuchung des Abdomens Rontgen Lab Prax 10 (1957) 234

WELIN S Modern trends in diagnostic roentgenology of the colon Brit J Radiol 31 (1958) 453

ZIMMERMANN H Die Verwendung von Kontaktlaxantien bei der rontgenologischen Untersuchung des Dickdarms Fortschr Rontgenstr 86 (1957) 245

the range of the latency was 1 to 75 min This concurs with the experience of other workers (ZIMMERMANN 1957, MIES 1957, EKLOF 1958) There were occasional cases in which the patient complained of abdominal pain at night and of somewhat disturbed sleep Nausea occurred in 5 % of cases

Effect of the patient's age on the evacuation result The influence of the patient's age on the result of the evacuation was investigated 213 patients belonged to the age group 20—40 years, 257 to the 40—60 years age group and 97 patients were over 60 years of age The percentage distribution was about equal in all three groups It appears that the patient's age has no obvious influence on the evacuation result

Effect of the time lapse after evacuation on the volume of gas in the colon A further routine film was taken in 175 cases one hour after the first in order to find out whether and to what degree the distribution of gas in the alimentary canal was affected by this delay In these 175 cases, as well as in all the other cases of this material, the patients were ambulatory The patients were examined erect, an examination performed with the patient recumbent would very probably have produced a different distribution of gas, but this has not been more closely investigated in connection with the present work

There was an equal incidence of increase and decrease in the amount of gas in the stomach in a third of the cases If the gas in the stomach diminished, the amount of gas in the small intestine or the colon, sometimes in both, always increased The volume of gas in the small intestine changed during the interval in 23 % of the cases and with few exceptions it increased The amount of gas increased in the colon in 34 % of the cases and it never diminished The changes in volume were about the same in all groups in all parts of the alimentary tract

Conclusions

The preparation of the colon with castor oil and a water enema, castor oil and a Clysodrast Novum enema, and a tablet and suppository contact laxative of the dioxyphenylisatin type (the substance which is also contained in Clysodrast) was compared in a material of 567 patients

Tablets and suppositories gave the best results and were the most convenient The enemas were given in the wards, probably the principal reason for the results being rather poor With a trained staff, however, it is also possible to achieve good evacuation results with a Clysodrast Novum enema and this agent is used in the author's department prior to any double contrast medium studies of the large bowel

The age of the patient had no effect on the evacuation result The roentgen examination should be started as soon as possible after the colonic evacuation, a delay of one hour increased the volume of gas in every third patient

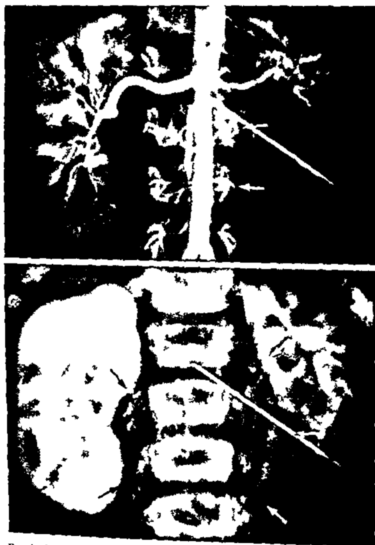


Fig 1 Lumbar aortography Large right kidney with slightly irregular upper pole Normal arterial and nephrographic phases Small left kidney with thin cortex and reduced vascular supply Two tumour like structures lie immediately below the narrow left renal artery (top picture) Numerous tortuous vessels are evident to the right and left of L2 and L3 and within a clearly defined zone in front of these vertebrae (lower view)

Lumbar aortography (Fig 1) Two *tumour* like structures the size of a walnut and of a pea respectively were evident close to the *aorta* *immediately* below the left renal artery Fairly wide tortuous vessels and a collection of contrast medium were evident *in these regions* and to a less extent in front of L2 and L3 and to the right of the aorta at the same level The

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CONTRAST MEDIUM ACCUMULATION IN PARA AORTIC LYMPH NODES DURING LUMBAR AORTOGRAPHY

Report of a case

by

HERMAN LODIN

Lumbar aortography is of considerable importance in the differential diagnosis of the causes of hypertonia, both with regard to the demonstration of tumours (phaeochromocytomata) producing this condition and in the identification of changes in the renal tissues and vessels

The following case has features of interest concerning the differential diagnosis of para aortic tumours in which abnormal vessels are demonstrable

A boy aged 9 years had when 6 months and again when 18 months old had acute pyelitis Following the attacks the Heller test for albumin had for many years occasionally been positive the blood pressure recorded when he was 6 years old was 160/110 When admitted for investigation the blood pressure was 190/175 to 145/120 The non protein nitrogen was 33 mg % Heller s test was positive and Esbach s reaction 0 4 % The urinary sediment contained numerous red and white blood cells Renal concentration tests gave a figure of 1 014 the endogenous creatinine clearance was 101 ml the insulin clearance 113 ml the PAH clearance 106 ml, and the urinary catechol level was normal

Urography The right kidney was enlarged the left small Good function on the two sides The upper calyces of the kidneys were slightly dilated but not otherwise abnormal A double renal pelvis and ureter were present on the left side and the left renal cortex was markedly reduced (only about 2 mm in thickness)

Submitted for publication 31 August 1960

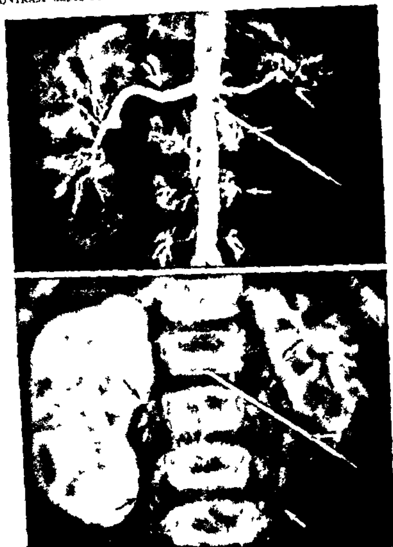


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Fig 2 Discrete highly vascular tumour adjacent to the left renal hilum An obvious accumulation of contrast medium is present and the structure is drained by a large vein (phaeochromocytoma)

right renal artery was wider than the left The right kidney was enlarged with the upper pole slightly irregular in shape The intrarenal vessels and the nephrographic effect were normal The left kidney was small and rather irregular in shape with few vessels the cortex in places was very thin The nephrographic effect was normal The adrenals showed a normal

vascular pattern and were of the usual size The investigation thus disclosed highly vascular para aortic tumours and fibrosis of the left kidney

Operation A series of tumours with the macroscopic appearances of lymph nodes were evident along the aorta corresponding in position to those demonstrated on aortography The left kidney presented the changes seen after repeated attacks of pyelonephritis and was removed Microscopic examination proved the para aortic tumours to consist of lymph nodules with slight, unspecific changes the left kidney showed evidence of pyelonephritis

Following operation the blood pressure fell to 125/120—95 80 indicating that the left kidney had been responsible for the hypertonia

Discussion

Tumours giving rise to hypertonia may be found at sites other than the adrenals and then commonly adjacent to the aorta (cf Fig 2) Abnormal vessels and an abnormal accumulation of contrast medium may occur in these tumours EDSMAN (1957) reported pathologic vessels in one case and an accumulation of contrast medium in another in 3 cases of phaeochromocytomata ELFVIN (1959) collected from the literature 8 phaeochromocytomata (including EDSMAN s) and discussed them together with a new case of his own, of these 9 tumours 7 had pathologic vessels Abnormal vessels may also be found in other tumours of the adrenal region, namely malignant adenomata, malignant neurinomata and neuroblastomata

Our case had pyelonephritic contracture of the left kidney which alone would account for the hypertonia, the urinary catechol level was normal The finding of para aortic tumour like structures on aortography was a further indication for operation, the fact that the structures were bilateral suggested that they were not connected with the pathologic left kidney

The tumour like structures were identified as lymph nodes and showed slight unspecific inflammatory changes there was no evidence of malignancy The roentgenographic demonstration of vessels in lymph nodes must be very rare and, as far as I am aware has not previously been reported LINDGREN however, has in two cases observed pathologic vessels in lymph nodes invaded by tumour tissue from a hypernephroma

The presence of the vessels demonstrated in the present case must have been caused by hyperaemia connected with slight inflammatory changes in the lymph nodes although it is remarkable that hyperaemic lymph nodes may contain filled tortuous vessels and an accumulation of contrast medium even though there is no question of malignancy It would therefore appear that this possibility must be borne in mind in considering the differential diagnosis

SUMMARY

A case is described in which filled tortuous vessels were evident in the para aortic lymph nodes on lumbar aortography The condition proved to be due to hyperaemia The implications as regards the differential diagnosis are discussed

ZUSAMMENFASSUNG

Es wird ein Fall beschrieben, bei dem mittels lumbaler Aortographie geschlängelte Gefässe in den para-aortischen Lymphknoten dargestellt werden konnten. Dieser Befund scheint auf Hyperämie zu beruhen. Die Bedeutung dieses Falles, soweit er die Differenzialdiagnose betrifft, wird diskutiert.

RÉSUMÉ

L'auteur présente un cas d'aortographie lombaire où des vaisseaux tortueux situés dans les ganglions lymphatiques para-aortiques ont été injectés et mis en évidence. Il s'est avéré que cet aspect est dû à l'hyperémie. L'auteur en étudie les conséquences au point de vue du diagnostic différentiel.

REFERENCES

EDSMAN, G.: Angionephrography and suprarenal angiography. Acta radiol. (1957) Suppl. No. 155.

ELFVIN, P.: Roentgen findings in a case of phaeochromocytoma. Acta radiol. 52 (1959) 461.

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PNEUMONOPLEURAL AMYLOID TUMOUR

Report of a case

by

P LUNDIN, B SIMONSSON and T WINBERG

A fundamental distinction should be made between primary amyloidosis which has no known cause or predisposing factors and secondary amyloidosis which accompanies chronic infectious or degenerative processes (HERXHEIMER and REINHARDT) This classification however does not cover all forms of amyloidosis The following four subdivisions of the condition were proposed by REIMANN et coll (1) Primary amyloidosis (2) Secondary amyloidosis (3) Amyloidosis accompanying myeloma and (4) Amyloid tumour

Categories (1) and (4) may be graded as primary amyloidosis as defined by HERXHEIMER and REINHARDT The first category is characterized by deposits of amyloid usually diffuse in several organs such as the heart, muscles skin intestines tongue and respiratory tract The fourth category takes the form of tumour like circumscribed multiple or solitary foci confined to a single organ system usually the respiratory tract or skin

Categories (2) and (3) are in principle secondary amyloidosis In category (2) the most common variety the amyloid deposits are generally found in the spleen liver kidneys and adrenals in myeloma category (3) the deposits are usually encountered in the same organs and have the same features as in primary amyloidosis

Submitted for publication 25 August 1960

ZUSAMMENFASSUNG

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RÉSUMÉ

L'auteur présente un cas d'aortographie lombaire où des vaisseaux tortueux situés dans les ganglions lymphatiques para-aortiques ont été injectés et mis en évidence. Il s'est avéré que cet aspect est dû à l'hyperémie. L'auteur en étudie les conséquences au point de vue du diagnostic différentiel.

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It seems to be established that the amyloid deposits are composed chemically of a protein and a sulphate containing polysaccharide Some workers have identified the latter substance as chondroitin sulphuric acid, but this has not been verified by others Considering that the primary and secondary forms of amyloidosis to some extent exhibit different staining properties it is conceivable that the composition of the deposits differs from one type of amyloidosis to another BRAUNSTEIN and BUERGER claim that three components are identifiable protein carbohydrate (or glykoprotein) and acid mucopolysaccharide

Pulmonary amyloid tumours typically contain cartilaginous and osseous tissue as well as giant cells (GLAUSER) Some investigators interpret the cartilaginous tissue as bronchial wall residues (BERGMAN and LINDER)

Amyloid tumours are not very uncommon in the respiratory tract, over 100 cases being on record They are however rare in the pulmonary parenchyma and pleura we have been unable to find more than 14 cases of amyloid tumour in the pulmonary parenchyma and only one case (PROWSE) situated in the pleura

Case report

Woman aged 72 One sister had pulmonary tuberculosis and another sister died of lung cancer Mass chest roentgenography in 1946 apparently disclosed no changes but in 1952 another examination revealed the presence of a rounded opacity at the apex of the left lung at the level of the 3rd rib posteriorly It was interpreted as pleural thickening

The patient became hoarse and had a non productive cough in the spring of 1958 In October 1958 roentgen examination including tomography showed roughly rounded opacities about 3 cm in size at both apices (Fig 1) In addition a homogeneous opacity as large as a hazelnut was observed in the left pulmonary parenchyma close to the dorsal thoracic wall (Fig 2) Calcified deposits were present in one of the opacities on the left side (Fig 3)

Because of these findings the patient was transferred to the Lung Clinic for further observation She had no temperature on admission and no lymph nodes were palpable Culture of sputum on media for growing tubercle bacilli and inoculation of guinea pigs were unsuccessful The hemoglobin concentration and the differential white cell count were normal No pulmonary or cardiac abnormalities were found on physical examination The thymol turbidity test Meulengracht s reaction the prothrombin time the serum alkaline phosphatase level and the glutamine oxalacetic acid transaminase all lay within the ranges of normal variation There were no signs of albuminuria The highest erythrocyte sedimentation rate recorded was 47 mm an hour The electrophoretic pattern of serum proteins was entirely normal

In an attempt to secure additional diagnostic information artificial pneumothorax was induced on the right side Insufflation of air caused the lung except for an adherent apical portion to collapse (Fig 4) At thoracoscopy a sharply outlined yellow lobulated soft mass could be seen protruding from the parietal pleura on the cupola at the side of the adhesions A similar mass was evident in the corresponding part of the lung A biopsy specimen was excised from the parietal protrusion Bronchoscopy was planned but refused by the patient

Biopsy findings The specimen consisted of a firm greyish white nearly homogeneous mass Microscopically the tissue was mainly composed of rounded nodules of a faintly laminated hyaline tissue and situated immediately below the pleural mesothelium in parts bulging out over the surface in coarsely papillar formations The vascular walls were everywhere considerably thickened by similar hyaline tissue Abundant cellular infiltrations were present perivascularly



Fig 1



Fig 2

Fig 1 Homogeneous opacities up to 3 cm in diameter at both apices Above they merge imperceptibly with the soft tissues of the thoracic wall and are convex and polycyclic in outline A similar opacity lightly larger than the end of a thumb lies near the right lateral chest wall and another the size of a hazelnut in the parenchyma on the left side

Fig 2 Tomography in a p and lateral projections Hazelnut sized parenchymal opacity at level of 3rd rib in left dorsal region

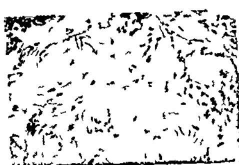


Fig 5 Subpleural amyloid deposits in nodules and vascular walls

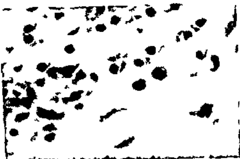


Fig 6 Infiltrations of plasma cells in the neighbourhood of the amyloid deposits.

We were unable to arrive at a conclusive diagnosis from the roentgen findings We were most inclined to believe that it was a matter of differentiating between tumours and inflammatory conditions, most probably tuberculosis The rounded process in the pulmonary parenchyma alone might well be caused by a tuberculoma or a tumour On the other hand the pleural lesions with their polycyclic outline and broadly based connection with the thoracic wall resembled neither a tuberculous process nor an ordinary pulmonary carcinoma or mycetoma Tuberculous infiltrations of the lungs may be situated subpleurally but would hardly have such a broadly based attachment to the pleura A pleural reaction to a tuberculous parenchymal process is admittedly common and may have a somewhat irregular shape but it would scarcely have so markedly a polycyclic demarcation from the lung as in this case Pleural tumours such as sarcoma mesothelioma and metastases will often give rise to pleural effusions Similarly situated malignant tumours, whether they arise from the pleura, the pulmonary parenchyma or the thoracic wall are often accompanied by pain and by destruction of neighbouring ribs and perhaps by manifestations due to pressure on the sympathetic trunk in the neck Benign tumours seldom merge so broadly with the soft tissues of the thoracic wall The bilateral presence of these lesions make it unlikely that they were associated with a malignant primary tumour

Since so few cases of amyloid tumour of the lung have been reported and fewer still include roentgen findings none of the roentgenologic features can be regarded as typical It may be that pneumonopleural amyloid tumours are rather less rare than the literature would seem to indicate The fact that amyloid tumours of this type have not been diagnosed more often in the past may have been due to their being diagnosed 'atypical tuberculous processes The need for further investigations such as thoracoscopy with biopsy in cases like this is apparent



Fig 3 Tomography Calcified deposits in opacity at left pulmonary apex



Fig 4 An opacity about 0 5 cm in diameter (arrow) persists parietally after right artificial pneumothorax

and in the neighbourhood of the hyaline nodules, predominantly plasma cells occasional reticular cells and some histiocytic cellular elements were found No giant cells could be seen There were no signs of cartilage formation or ossification (Figs 5 and 6) Slides stained with methyl violet or crystal violet showed small areas which were distinctly metachromatic limited areas had a definite positive periodic acid Schiff reaction Whereas the entire specimen was faintly stainable with Congo red no distinct metachromasia was found in slides stained with toluidinblue

Seven months after discharge from hospital the patient had no symptoms or signs referable to the lungs and the roentgen appearances were unchanged

Discussion

The essential pathologic criteria of an amyloid tumour are satisfied by the case described In some respects the staining properties of the amyloid deposit deviated from those characterizing the common form of secondary amyloidosis (cf BRAUNSTEIN and BUERGER)

The clinical picture is also consistent with that seen in cases of amyloid tumour For example, there is no history of previous disease and the site strongly suggests that this is not a case of a secondary amyloid tumour The possibility cannot, of course, be ruled out that amyloid deposits are present in other organs, but there are no evidences suggesting that this is the case

As in other cases of amyloid tumour published so far, our case is characterized by few symptoms The cough which was the main reason for sending the patient for roentgen examination was not particularly severe and in due course disappeared, it may have been only a manifestation of a stubborn cold Often centrally located tumours will give rise to a cough, while more peripheral ones, as a rule, are unaccompanied by symptoms

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DISTRIBUTION OF RADIOACTIVE IRON IN PREGNANT MICE STUDIED BY WHOLE BODY AUTORADIOGRAPHY

by

SVEN ULLBERG, BO SORBO and CARL JOHAN CLEMEDSON

The distribution of radioactive iron in the animal body has been previously investigated by means of autoradiography or impulse counting (COPP and GREENBERG 1946, ZILIOTTO and ODEBLAD 1955, AUSTONI, ZILIOTTO and ODEBLAD 1956, FERRINI et coll. 1957), but the technique used in the present work has the advantage of giving a general survey of the uptake of the isotope in the entire body. It also allows the detection of an accumulation of the isotope in a large number of tissues and organs that are usually not included in conventional autoradiographic methods on dissected organs. Pregnant animals were used in our investigation with the aim of studying the distribution of the iron in the mother and fetus at various times after the administration.

In addition to the general interest of an elucidation of iron metabolism, and the utilization of iron by the body in iron therapy, the present work was also initiated by the consideration of a possible occurrence of radioactive iron isotopes in bomb debris from nuclear explosions and following severe

Submitted for publication 22 July 1960.

SUMMARY

A case of amyloid tumour in the pulmonary parenchyma and pleura is reported The clinical picture, differential diagnosis and pathologic features are discussed

ZUSAMMENFASSUNG

Ein Fall mit Amyloidtumor im Lungenparenchym und in der Pleura wird berichtet Das klinische Bild, die Differentialdiagnose und die pathologischen Züge werden diskutiert

RÉSUMÉ

Les auteurs présentent un cas de tumeur amyloïde du parenchyme pulmonaire et de la plèvre Ils étudient le tableau clinique, le diagnostic différentiel et l anatomie pathologique de cette affection

REFERENCES

BERGMAN F and LINDER E Tumor forming amyloidosis of the lung J thorac Surg 35 (1958), 628

BRAUNSTEIN H and BUERGER L A study of the histochemical and staining characteristics of amyloid Amer J Path 35 (1959) 791

GLAUSER O Über tumorförmiges Amyloid der Lungen Schweiz Z allg Path 18 (1955) 12

HERXHEIMER, G und REINHARDT A Ueber lokale Amyloidosis Berl klin Wschr 50 (1913) 1648

PROWSE C B Amyloidosis of the lower respiratory tract Thorax 13 (1958) 308

REIMANN H A KOUCKY R I and EKLUND C M Primary amyloidosis limited to tissue of mesodermal origin Amer J Path 11 (1935) 977

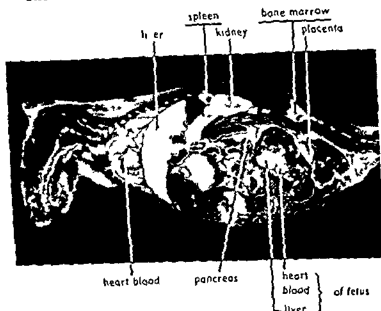


Fig 2 Autoradiogram Distribution of Fe^{59} in a mouse 20 min after intravenous injection High activity in liver bone marrow and red pulp of spleen of the mother Higher concentration of Fe^{59} in the blood of fetus

killed after 2 and 10 hours, respectively Another group containing 3 animals was given 1 0 $\mu C/g$ bodyweight of the isotope perorally by tube feeding These animals were killed in the same manner as the others after 4 hours, and 2 and 4 days

The animals were sectioned and autoradiograms were prepared according to the method developed by ULLBERG (1954 1958) Sagittal sections 20 μ thick through the whole animals were made at different levels The sections were dehydrated at —10 C and autoradiograms prepared by apposition against Gevaert Dentus Rapid film and with an exposure time of about 7 days in the first group and about 12 days in the second group

Results

In the presentation of the results the distribution of radioactivity in the mother and in the fetus with surrounding uterus wall fetal membranes and amnion fluids will be treated separately

Intravenous administration of Fe^{59} — Distribution in the mother Two minutes after the intravenous injection all the radioiron appears to be retained in the blood The autoradiograms obtained at that time show almost identical

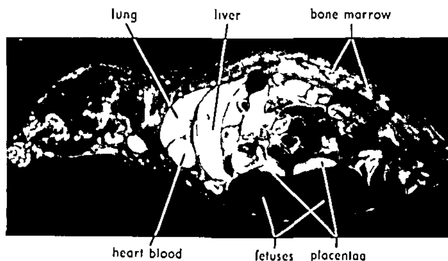


Fig. 1. Autoradiogram. Distribution of Fe^{59} in a mouse 5 min after intravenous injection of the isotope. White areas correspond to high concentration of radio iron. The isotope is mainly confined to the blood but a commencing accumulation may be noticed in the bone marrow and liver of the mother. A small amount of Fe^{59} has been taken up by the fetal blood, liver and bone.

nuclear reactor accidents, the radioactive iron may be due to neutron activation of construction details of the nuclear device or reactor shielding.

A preliminary report of this investigation was presented at the Scandinavian Summer Meeting on Biochemistry, Medical Chemistry, Pharmacology and Physiology in Turku, Finland, August 27—29th, 1959.

Methods

The Fe^{59} was obtained from the Radiochemical Centre, Amersham, England, in the form of $FeCl_3$ in 0.1 N HCl. The specific activity was in two different shippings of isotope 15 and 63 mC/mg, respectively. The ferric chloride was converted to citrate by the addition of 1 ml of 0.05 mole trisodium citrate to the isotope solution and evaporation of the latter to dryness. The residue was dissolved in distilled water and this solution was used for the injections and other administrations.

Pregnant mice, weighing from 22 to 39 g, were employed as experimental animals. One group consisting of 11 animals was used for the intravenous administration of the isotope, 0.5 μC/g bodyweight (corresponding to 0.008 to 0.03 μg Fe/g bodyweight) being injected into a tail vein. The injected volume was 0.01 ml/g body weight. These animals were anaesthetized and killed by immersion in a carbon dioxide acetone mixture (—78° C) at 2, 5 and 20 min, and 1, 4 and 24 hours, and 3 and 6 days, after administration of the isotope. In two animals radioiron was injected subcutaneously, these animals being

tract and bladder or in the central nervous system (with the exception of the choroid plexus)

At 4 hours after the injection (Fig 4) when the activity in the blood has reached its minimum the highest concentration of radioiron is found in the bone marrow The organs may at that time be ranged according to their degree of activity as follows

High activity bone marrow dental enamel, choroid plexus, red pulp of spleen liver

Medium activity the mammary glands pancreas, gastric mucosa intestinal mucosa salivary glands, thyroid pituitary gland

Low activity lung kidney myocardium, lymph nodes and thymus, skeletal muscle gastric and intestinal contents, blood and brain (with the exception of the choroid plexus)

As is seen in Fig 5 the highest activity in the bone is found in the marrow but some activity is also evident in the compact bone, where it is mainly located subperiosteally

The radioactivity in the liver is located essentially in the central parts of the lobuli In the gastric and intestinal mucosa the highest concentration of radioiron is found in the basal layer The activity in the gastric mucosa seems to be associated chiefly with the zymogenic cell layer The activity in the lumina of the stomach and the intestine is very low and there are no signs of excretion of radioiron The bile ducts and the pancreatic duct also have a very low radioactivity In the kidney, where the overall activity is about the same as in the blood the activity is confined mainly to the cortex and is very low in the medulla There are no signs of any excretion of radioiron to the surface of the skin

Ten hours after the injection the activity in the blood is still rather low although somewhat higher than after 4 hours The increasing concentration of radioiron in the blood obviously must be due to the commencing liberation of red cells containing radioactive hemoglobin (HAHN et coll 1939) At one day and later after the injection the characteristic feature of the autoradiograms is the increasing concentration of Fe^{59} in the blood Three days after the administration of the isotope the activity in the blood is still somewhat lower than in the bone marrow After 6 days, however the activity is higher in the blood than in the bone marrow which indicates that the majority of red cells containing radioactive iron have already left the latter The activity decreases earlier in the liver than in the bone marrow In the red pulp of the spleen the concentration of radioiron remains high for a considerable time The dental enamel retains a high activity throughout the time of observation

Three days and 6 days after the administration of the isotope an accumulation of Fe^{59} can be observed in the brown fat tissue The activity in the mammary gland, on the other hand has decreased at that time

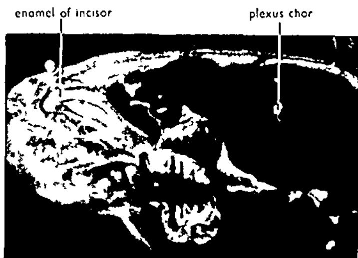


Fig 3 Autoradiogram Fe^{59} distribution in head of a mouse 1 hour after intravenous injection High activity in teeth especially in the enamel of incisors and in the choroid plexus

appearances to those produced with the same technique and showing the distribution of I^{131} tagged serum albumin (ULLBERG, unpublished experiments) Five minutes after the injection (Fig 1), some initial accumulation is evident in the bone marrow, liver, and red pulp of the spleen but the bulk activity *still* lies in the blood

Twenty minutes after the injection (Fig 2), the activity in the blood has decreased while the concentration in the hematopoietic organs has increased so that they stand out more distinctly The teeth now show a very high concentration The activity is mainly confined to the enamel of the incisors, whereas the dentin exhibits a fairly low concentration, the dental pulp has a somewhat higher activity than the blood Other organs — the placenta and fetus being excepted — have a considerably lower activity The concentration in the pancreas is somewhat higher than in the blood, and the basal layer of the mucosa of the stomach and intestine displays a Fe^{59} concentration that is about the same as that of the blood

At one hour after the injection the activity in the blood has undergone a further considerable decrease In addition to the very high activity in the dental enamel (Fig 3) and the hematopoietic organs, the pancreas and the gastric and intestinal mucosa have a rather high concentration A surprisingly high activity is found in the choroid plexus (Fig 3) and in the mammary glands Parts of the latter appear in Fig 4 in the ventral and dorsal region of the neck due to the special arrangement of these glands in small rodents In the pituitary and thyroid glands the amount of radioiron is lower, although it is greater than in the blood Practically no activity is to be seen in the lymphatic tissue, thymus, the white pulp of the spleen, lymph nodes, urinary

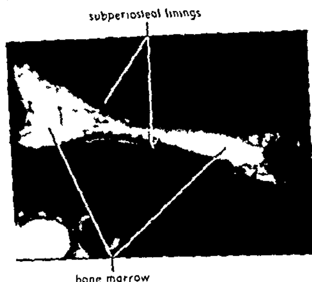


Fig 5 Detail from fig. 4 showing uptake of radioiron in bone marrow and in subperiosteal lining of a pelvic bone

Peroral administration of Fe^{59} The distribution patterns after peroral administration were largely similar to those after intravenous injection One notable exception however is that the radioiron did not accumulate in the liver of the mother (Fig 6) the concentration in the liver being lower than in the blood In the liver of the fetus, on the other hand, an appreciable accumulation was seen and the concentration appeared to be of the same magnitude as in the cases of intravenous injection

Four hours after the administration rather large amounts of the isotope were still present in the intestinal contents while at later times the radioiron content of the intestines was only insignificant

Subcutaneous administration of Fe^{59} The distribution of radioiron in the mother after subcutaneous administration of the isotope was also essentially similar to that after intravenous injection A remarkable observation however, was that as in the case of peroral administration the uptake in the liver was very low or almost nil

Discussion

The present investigation clearly demonstrates that the radioiron is leaving the blood stream and is taken up in the tissues rather slowly in comparison with other metabolites such as amino acids which are almost completely cleared off from the blood within the first ten minutes after their intravenous administration

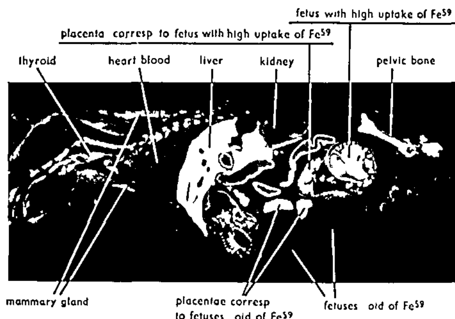


Fig 4 Autoradiogram Distribution of Fe^{59} in a mouse 4 hours after intravenous injection Almost all the isotope has left the blood Two fetuses show no uptake of radioiron the corresponding placentae have an extraordinarily high radioactivity

Distribution of Fe^{59} in the fetus No radioactivity has been found in the fetus at 2 min after the injection, but traces of activity which are confined to the blood and the liver and fetal bone are evident after 5 min As early as 20 min the concentration of radioiron in the blood of the fetus is higher than that in the blood of the mother, and the fetal blood activity thereafter remains considerably higher than in that of the mother during the whole observation period

The distribution of the isotope in the fetus is different from that in the mother in the following respects The activity in the liver is much more dominating in the fetus than in the mother, the fetal bone marrow displays a comparatively low activity especially in the central parts of the marrow, and the central nervous system of the fetus has a higher uptake than that of the mother The high activity in the fetal liver is probably due to its hematopoietic function The accumulation of radioiron in the choroid plexus of the fetus is remarkably high

The placenta shows a fairly high uptake immediately after the injection, and it still retains a high concentration 24 hours after the administration

In the mice killed up to 20 min after the injection the activity is fairly evenly distributed in the chorio allantoic placenta, but later on an additional still greater accumulation appears on the inner margin facing the fetus and which seems to correspond to the visceral yolk sac epithelium

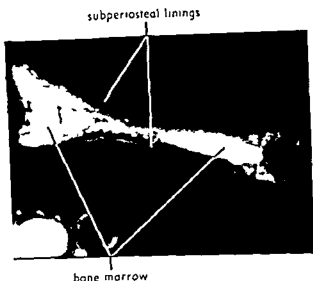


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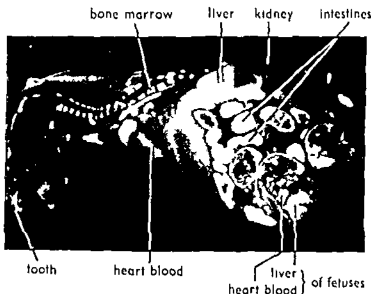


Fig. 6. Autoradiogram. Distribution of Fe^{59} in a mouse 4 hours after peroral administration. Low uptake in maternal liver but high uptake in fetal liver. High content of radioiron is still present in the intestine.

The general distribution patterns of radioiron in the body found in this study is, as far as the blood and the hematopoietic organs and the intestinal mucosa are concerned, essentially in agreement with the results obtained by other investigators by means of impulse counting or autoradiography on dissected organs (HAHN et coll. 1939, AUSTONI and GREENBERG 1940, GRANICK and HAHN 1944, COPP and GREENBERG 1946, AUSTONI, ZILIOTTO and ODEBLAD 1956). The high concentration of the isotope which could be demonstrated in some other organs, however, merits some discussion.

The considerable accumulation of iron in the teeth is of particular interest. The rapid uptake of the isotope from the blood stream in this tissue seems to indicate that the iron in the teeth is present essentially in the inorganic form. The isotope lies especially in the enamel, and it should be noted that its distribution in the teeth shows a picture similar to that of radiostrontium and other bone seeking isotopes (ENGSTRÖM et coll. 1958). It has been demonstrated earlier that the incisors of rodents have a fairly high content of iron but its physiologic significance is not known.

The heavy uptake of radioiron in the choroid plexus is of great interest as regards the possible metabolic function of this structure. The physiologic significance of the high iron uptake of the plexus is, however, unknown.

Of particular interest is the high concentration of radioiron found in the salivary, mammary, thyroid and pituitary glands. As far as the three first mentioned glands are concerned, their high iron uptake may perhaps be related to

their known content of peroxidase (ASTWOOD 1955). In comparison with other iron sources in the body, however, enzyme iron represents only a small part, probably less than one per cent. Nothing seems to be known so far about the physiological role of the iron in the pituitary gland. The fairly high uptake of radioiron by the pancreas, which was demonstrated earlier by ZILIOTTO and ODEBLAD (1955), has been confirmed by the present study.

TUBIANA *et coll.* (1959) found a high concentration of parenterally administered radioiron in the intestine and suggested an intestinal cycle with secretion and re-absorption of the isotope. The present investigation does not support these findings. In accordance with COPP and GREENBERG (1946) we found no appreciable excretion to the intestinal lumen of injected radioiron. Nor has any significant excretion been found to take place through other possible routes, such as through the kidneys, biliary and pancreatic ducts or to the surface of the skin.

The observed distribution of Fe^{59} in the placenta and fetus is in large in agreement with the results of other investigators (VOSBURGH and FLEXNER 1950, CAMPBELL and NYLANDER 1951, NYLANDER 1951, 1953, VON EHRENSTEIN and HEVESY 1956, DAVIES et coll. 1959).

The fact that the fetal blood has a considerably higher concentration of radioiron than the maternal blood as early as 20 min after the injection is in accordance with the findings of VOSBURGH and FLEXNER (1950). They suggested that iron is transferred from mother to fetus as serum iron and that the maternal red cells are not an important source for the fetal iron. It also seems to speak in favour of the passage of iron through the placenta being an active process.

A peculiar finding in the autoradiogram of one animal that was killed 4 hours after the injection of the isotope was that two of its fetuses had taken up no activity at all. The corresponding placentae, on the other hand, showed a very high concentration of radioiron, their activities being several times higher than the activity found in those fetuses that had taken up radioiron in the usual extent. The microscopic appearance of those fetuses that did not show any uptake of radioiron was normal and did not differ from the others in respect to size and stainability, for example. No explanation for this placenta-fetus blockage to iron passage could be found. It should be noted in this connection, however, that VOSBURGH and FLEXNER (1950) have found that there may be a considerable difference in the amount of iron transferred to members of the same litter during the course of an experiment.

The strong accumulation of radioiron in the fetus is of significance from the standpoint of radiation hazards in human iron metabolism studies with radioactive iron and in accidental exposure. The most potent isotope is Fe^{59}, which is classified as highly dangerous, while Fe^{55} is classified as dangerous. The critical organ of the fetus for radioiron seems to be the liver, which has an important hematopoietic function in the fetus. As shown by VON

EHRENSTEIN and HEVESY (1956), 73 to 83 per cent of the total iron content of the fetus is located in the liver In the adult, the gastrointestinal tract and the spleen are listed as the critical organs (ICRP 1959)

In addition to the bone marrow which is highly radiosensitive in the mother as well as in the fetus, the choroid plexus and the placenta should be kept in mind as possible critical points since it is probable that the corresponding structures in the human subject also have the ability to concentrate radio iron

The maximum permissible total body burden for Fe^{59} according to the recommendations of the ICRP (1959) is 20 μC For iron metabolism studies by means of radioactive iron VLALL and VETTER (1958) state that after a dosage of 20 μC to an adult person, the total dose will not exceed 1 5 rad distributed over a time interval of 9 weeks

SUMMARY

Fe^{59} was administered intravenously and in a few experiments perorally and subcutaneously to groups of pregnant mice, and the distribution studied in sections of the whole animals by an autoradiographic technique The uptake of the iron in the organs of the mother and fetus at various intervals is described and discussed

ZUSAMMENFASSUNG

Gruppen schwangere Mäuse erhielten Fe^{59} intravenos und in wenigen Experimenten peroral und subkutan Die Verteilung des Isotopen wurde in Sektionen des ganzen Tieres mit Hilfe einer autoradiographischen Technik studiert Die Aufnahme des Eisens in den Organen der Mutter und des Fotus zu verschiedenen Zeitpunkten der Schwangerschaft wird beschrieben und diskutiert

RÉSUMÉ

Du Fe^{59} a été administré par voie intraveineuse et dans quelques cas par voie buccale et sous cutanée a des groupes de souris gravides sa répartition a été étudiée sur des coupes totales du corps de ces animaux par une technique autoradiographique Les auteurs décrivent et étudient la fixation du fer dans les organes maternels et foetaux à différents stades

REFERENCES

ASTWOOD E B Mechanism of action of antithyroid compounds Brookhaven Symposia in Biol 7 (1955) 61

AUSTONI M E and GREENBERG D M Studies in iron metabolism with the aid of its artificial radioactive isotope The absorption excretion and distribution of iron in the rat on normal and irondeficient diets J biol Chem 134 (1940) 27

— ZILIOTTO D and ODEBLAD L Thyroid and iron metabolism I A study on ^{59}Fe uptake in the bone marrow and in different organs of thyroidectomized rats using scintillation counting and autoradiography Acta med scand 155 (1956) 329

CAMPBELL D and NYLANDER G Studies on the placental transfer of iron by means of track autoradiographic technique using Fe^{59} Acta physiol scand 23 (1951) 196

COPP D H and GREENBERG D M A tracer study of iron metabolism with radioactive iron I Methods Absorption and excretion of iron II Internal metabolism J biol Chem 164 (1946) 377 and 389

DAVIES J BROWN Jr E B STEWART D et coll Transfer of radioactive iron via the placenta and accessory fetal membranes in the rabbit Amer J Physiol 197 (1959) 87
VON EHRENSTEIN G and HEVESY G Embryonal iron turnover Acta physiol scand 38 (1956) 184
ENGSTROM A BJORNERSTEDT R CLEMEDSON C J and NELSON A Bone and radiostrontium Almqvist och Wiksell Stockholm and John Wiley and Sons New York, 1958
FERRINI O PALMIERI A PERRONI G L and BIASSONI P Distribution of radioiron in rabbit with particular reference to the digestive tract Arch E Maragliano Pat Clin 13 (1957) 23 Quoted from Chem Abstr 51 (1957) 9758
GRANICK S and HAHN P F Ferritin VIII Speed of uptake of iron by the liver and its conversion to ferritin iron J biol Chem 155 (1944) 661
HAHN P F BALE W F LAWRENCE E O and WHIPPLE G H Radioactive iron and its metabolism in anemia Its absorption transportation and utilization J exp Med 69 (1939) 739
INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION Report of Committee II on permissible dose for internal radiation (1959) Recommendations Pergamon Press London 1959
NYLANDER G Studies on the iron in the yolk sac of the pregnant rat in normal and anemic conditions Acta Soc Med upsalien 56 (1951) 11
— On the placental transfer of iron An experimental study in the rat Acta physiol scand 29 (1953) Suppl 107
TUBIANA M PELLERIN P et SIROUX, M R Étude de la distribution du fer radioactif chez la souris par autoradiographie anatomique a —195 C C R Acad Sci 249 (1959) 2875
ULLBERG S Studies on the distribution and fate of S^{35} labelled benzylpenicillin in the body Acta radiol (1954) Suppl No 118
— Autoradiographic studies on the distribution of labelled drugs in the body Proc Second UN Internat. Confer Peaceful Uses Atomic Energy 24 (1958) 248
VEALL N and VETTER H Radioisotope techniques in clinical research and diagnosis. Chapter 14 Butterworth, London 1958
VOSBURG G J and FLEXNER L B Maternal plasma as a source of iron for the fetal guinea pig Amer J Physiol 161 (1950) 202
ZILIOTTO D and ODEBLAD E Uptake of injected radioiron in some digestive organs of mice Acta med patav 15 (1955) 207

Book reviews

STRAHLENBIOLOGIE, STRAHLENTHERAPIE, NUKLEARMEDIZIN UND KREBSFORSCHUNG Ergebnisse 1952—1958 Herausgegeben von H R Schinz, H Holthusen, H Langendorff B Rajewsky und G Schubert 998 Seiten, 395 Abbildungen und 140 Tabellen Georg Thieme, Stuttgart 1959 Price DM 275

With the object of carrying on the tradition from Ergebnisse der medizinischen Strahlenforschung, of providing radiotherapists and radiobiologists with reviews of the developments in their special fields this book presents a series of short monographs on subjects related to radiobiology, radiotherapy nuclear medicine and cancer research

Four chapters are devoted to radiogenetics and one chapter presented in readily comprehensible terms by WIDLROE the designer of the Asclepitron, deals with the physics and technique of megavolt radiation Experiences with the 31 MeV betatron in Zurich, described by COCCHI should be of interest to all working with million volt treatment The chapter on radiomimetic substances is rather short and would have been more complete if it had contained case reports and photographs of patients taken before and after treatment

The treatment of bronchial cancer by radiation is discussed by HELLRIEGEL who also describes three cases of lung cancer in which the patients were alive three years after treatment Isotope diagnosis in diseases of the thyroid gland is described exhaustively by HORST and isotope treatment by GAUWERKY both from Hamburg

The work may be regarded as a reference book with an extensive bibliography

Folke Jacobsson

CINEFLUOROGRAPHY Proceedings of the First Annual Symposium on Cinefluorography 1958 Edited by G H S Ramsey J S Watson T A Tristan S Weinberg and W S Cornwall 266 pages 142 figures and 8 tables Charles C Thomas Springfield, Ill 1960

Considerable interest is shown by radiologists and others in cinefluorography for evaluating normal and abnormal anatomy and physiology The First (1958) Annual Symposium on Cinefluorography at the University School of Medicine and Dentistry Rochester was well attended and the Proceedings form an attractive book being of special value as both elementary problems and latest developments have been included

The answers to questions during the discussion following the various papers have been carefully edited and thus the complete discussion can be followed — an arrangement providing much of value to the reader

In the introductory chapters a general view of the methods of cinefluorography image intensification and the application of television to cinefluorography are presented Recording equipment and photographic aspects are also considered and the problem of the radiation dose in image intensifier cinefluorography is discussed Special chapters are devoted to the projection and diagnostic analyses of cinefluorograms

Not only are more conventional methods of cinefluorography discussed but new and more special procedures such as the use of solid state amplifying screens fibre optics and less conventional image amplifiers are also considered The illustrations based on slides and thus of educational clarity as well as the printing are of very high class

The book provides concentrated information on the problems involved and is warmly recommended to all radiologists

Ove Mattsson

MEDICAL X RAY TECHNIQUE By G J van der Plaats 492 pages and 213 illustrations Philips Technical Library Eindhoven 1959 Price Sw Kr 41 50

This book is stated to be a text book for all concerned in the medical use of roentgen rays in diagnosis and therapy and particularly for student radiographers Both roentgen and isotope problems are treated The author of the book is wellknown to most radiologists and this exhaustive treatis on the principles and applications of medical roentgen technique bear the mark of solid knowledge

The production of roentgen rays roentgen tubes and the properties of roentgen rays are discussed in an introductory chapter The methods of image formation and laws of projection as well as resolution of detail and problems of definition are examined thoroughly The photographic problems including contrast exposure and processing are considered in separate chapters and different apparatus as well as radiographic techniques are exhaustively described electrical wiring diagrams are included The biologic effect of radiation dosimetry different types of radiation therapy and isotopes are discussed in turn The final chapter deals with the radiation hazards and protective measure in roentgen diagnosis and therapy

The book provides the reader with valuable information not only confined to routine practice Concentrated data of a more special character appear in small print But yet in some respects one misses more detail. Developing machines image intensifiers and cinefluorographic techniques have for example been dealt with rather summarily The illustrations are really excellent

This book is recommended to all who are entering roentgenology although it is also of value to others as a reference work No modern book of such a comprehensive nature has been available until now

Ove Mattsson

WILHELM CONRAD RONTGEN UND DIE GESCHICHTE DER RONTGENSTRAHLEN Von O Glasser Mit einem Beitrag Personliches uber W C Rontgen von M Boveri 2 Auflage 381 Seiten 112 Abbildungen Springer Verlag Berlin Gottingen Heidelberg 1959 Price DM 58

A second edition has now appeared of Dr O Glasser s well known book on W C RONTGEN and the history of roentgen rays A number of additions and improvements have been made but the main character of the book is unchanged The life of RONTGEN is reported as fully as available sources permit A long contribution by Miss M Boveri Personal data on W C Rontgen in which important and valuable information is mingled with *long versified* dinner speeches and other matters of limited interest is included Dr Glasser duly stresses the often forgotten fact that RONTGEN was a highly renowned physicist and had made important contributions *to science long* before the discovery of roentgen rays in 1895

The history of roentgen rays and their uses in various sciences including medicine technology and other spheres of activity are in this book mainly confined to the year 1896 from which year no *less than 1 044* books brochures and papers in scientific journals are listed The references from later years number 86 The reaction of the scientific world and of the *general public to the* discovery is described in great detail this is sometimes amusing but at times boring The reprints of RONTGEN s own three papers of the period 1895—1897 are *in a class by themselves* brief clear and concise It is surprising to see how much scientific and technologic progress of the following decades was anticipated in these early papers

Sten Benner

THE TOMOGRAM ITS FORMATION AND CONTENT By Paul Edholm 109 pages and 74 illustrations Acta radiol (1960) Suppl No 193 Sw Kr 30

This book is aimed at an analysis of the influence in tomography of the type of tomographic movement employed the size of the tomographic angle and the distance between the tomographic plane and the centre of the object as well as the absorption of the object

The apparatus radiation and film were standardized by the use of mathematic models so that curves showing the density distribution (the image relief) in the tomogram could be calculated These calculations were performed for circular and linear tomography of a sphere and a cylinder for different values of the factors enumerated above An electronic digital computer was employed The images represented by the calculated curves were assessed by applying physiologic principles underlying the perception of contour and contrast The variations of contour sharpness and contrast in the tomogram under different conditions are shown in the book by means of graphs It was possible to construct image relief curves for tomograms of other objects with the aid of the curves calculated for the sphere and cylinder

A quantitative assessment of the distortion of the image caused by tomography under various conditions was among the results obtained It was found that large tomographic angles considerably distort the image so that sharpness and contrast are much reduced when the object tomographed is a hollow organ with a thin wall this reduction of sharpness and contrast becomes marked

Discrepancies between the mathematic models used for the calculations and practical tomography are discussed and the effect of some of these are calculated

Tomograms were obtained experimentally under conditions corresponding as far as practicable to those for which the calculations were valid in order to test and supplement some of the theoretical conclusions densitograms that represented the image reliefs were made from the films Tomograms of spheres and cylinders were produced with commercial apparatus in a second series of experiments

Autoreview

LOW LEVEL IRRADIATION Edited by Austin M Brues 158 pages 18 illustrations American Association for the Advancement of Science Washington 1959 Price $ 3 75

This booklet consists of papers read at a symposium of the American Association for the Advancement of Science in cooperation with the U S Atomic Energy Commission and the Argonne National Laboratory in December 1957 In contrast to most other treatises of this nature the book deals not only with radiation levels and various biologic effects of radiation for almost as much space is devoted to their implications for human relations in general

The first part Scientific Background after a short introduction by F L POWERS begins with a paper by R E DUDLEY on natural and artificial radiation levels showing how little the much discussed fall out radiation means at least as yet in comparison to natural and medical radiation L MACHTA reviews meteorologic facts of importance for the distribution of radioactive fission products from nuclear weapons tests over the earth E L GREEN summarizes genetic effects and the editor deals with the somatic effects of radiation The difficult task of giving in the very limited space the essentials of what we know and what we need to know seems to have been very well solved

The second part Implications is introduced by the editor whereafter D F PRICE looks at the problems as a public health administrator from a non technical viewpoint A J SNIDER writes on the responsibility of the press to provide the public with well balanced information on these difficult questions C HOLIFIELD treats legal and political implications and C W CHURCH

MAN discusses the intricate problems of the morals of science. The book ends with a summary and conclusions by the Editor

The book is very well worth reading and is thought provoking as a general consideration from many different viewpoints of questions of great importance possibly in the future life or-death ones for humanity

Sten Benner

THE TREATMENT OF BRONCHIAL NEOPLASMS By Robert R Shaw and Donald L Paulson with a chapter on bronchial adenoma by John Lester Kee Jr 135 pages 63 illustrations and 10 tables. Charles C Thomas Springfield Ill 1959 Price $8

The authors of this book point out in the introduction that in spite of intensive propaganda for early diagnosis the operability figure for lung cancer has not shown much improvement during the past few years The number of operable cases is approximately the same among both early and late cases The authors consider that the time factor is of lesser significance than the biologic factors in the prognosis for lung cancer

The conclusions are based on a material of 1 180 cases of cancer of the lungs Approximately two-thirds of the cases were inoperable and consequently had to be treated by methods other than surgery Radiation treatment stood first as the method of choice in these cases mainly as a palliative measure The authors state that it was possible with radiotherapy to reduce or even entirely eliminate the atelectasis and hence bring considerable relief in the dyspnoea and cough Particularly in compression of the vena cava radiation treatment usually produced a rapid and as a rule permanent improvement in the troublesome symptoms

Naturally enough seeing that the authors are surgeons, the greater part of the book is devoted to a discussion of the selection of patients for operation and different operative methods One chapter however deals with the possibilities offered by radiotherapy in the treatment of lung cancer and contains good reproductions of roentgenograms taken before and after treatment An inoperable case given radiation treatment and alive six years later free from symptoms and at work, is described in some detail The roentgen technique employed for the treatment is not mentioned however A short chapter is devoted to chemotherapy and in conclusion the authors give a brief review of bronchial adenoma a tumour group which though small is of considerable interest from the biologic and differential diagnostic points of view

The book presents a clear picture of the treatment possibilities in cancer of the lungs together with both comprehensive and well reproduced illustrations

Folke Jacobsson

DETAILERKENNBARKEIT UND DOSIS BEI DER RÖNTGENDURCHLEUCHTUNG Von W Frik. Medizin Theorie und Klinik in Einzeldarstellungen Band 6 168 Seiten 35 Abbildungen und 48 Tabellen Alfred Huthig Verlag Heidelberg 1959 Price DM 18

This monograph deals with the ideal conditions for fluoroscopy of the chest with special reference to the dose and the information such an examination can yield

The experimental arrangement consisted of plexiglass or sugar paraffin bodies in the shape of Landholt s rings beads or truncated cones placed in front of or behind plexiglass phantoms or thin walled vin dur chambers containing water The initial roentgen factors employed were 55 kV and 3 mA with a total filtration corresponding to 2 mm Al This value was chosen on empiric grounds as the lowest possible for satisfactory fluoroscopic examination of the chest. The examination conditions were varied in different ways according to the filtration screen

emulsion, focus, type of generator and strength of voltage and current The most satisfactory combination was found to be 90 kV from a 6 valve apparatus 1 mA, and filtration corresponding to 6 mm Al The best fluoroscopic screen contained 100 mg ZnCdS per cm² with 62 5% ZnS In all examinations a focus screen distance of 70 cm was used Fluoroscopy under these optimal conditions gives a low skin dose and a low volume dose The percentage increase of the gonad dose is fairly high but the absolute gonad dose is nevertheless so small that it may be neglected

On fluoroscopy with a Philips 5 inch image intensifier it was found that the perception of well defined details was twice as good while less well defined details were not so readily recognised as in ordinary fluoroscopy The reduction of the radiation dose was very small Fluoroscopy with less than 1 mA and a focus screen distance of 70 cm involves the risk of very disturbing quantum fluctuations especially by dense objects

Unfortunately the language is inclined to be cumbersome and the author s meaning is not always clear in addition calculations and surveys of numeric data are rather scanty although they can be readily deduced from the information given But with these reservations it may be said that the views presented by the author are valuable and deserve consideration

Thure Holm

DIAGNOSTIC RADIOISOTOPES By Charles A Owen Jr 425 pages 71 figures and 49 tables Charles C Thomas Springfield, Ill 1959 Price $ 15 75

It is stated in the preface that the literature on medical applications of the radioactive isotopes is concerned primarily with treatment and only incidentally with the diagnostic tests This seems to be an overstatement for the reviewer recalls books even from the same publisher which were similar to the present one and in which the emphasis was on diagnostic usage Be that as it may the book is nevertheless quite valuable and to be recommended as a good introduction to modern radioisotope diagnostics Its use presupposes however some previous knowledge of radiation physics radiation detectors and radiation protection subjects which are but briefly treated Attention in the main is paid to a detailed description of the practical performance of the more important tests and on the calculation of the results

The matters most fully treated are the use of radioiodine for metabolic studies chromium and iron in hematology and the localization of tumours and long lists of references add to the usefulness In reading the longer chapters it is however rather difficult to find the references to the particular chapter as the chapter headings are not as is usual given at the top of the pages

A number of the other uses of radioisotopes are described more briefly although the references indicate to the interested reader where he can gather further information Tables of the known radioisotopes and of the decay of the more important ones at various times as well as of logarithms conclude the monograph

Sten Benner

ACTA RADIOLOGICA

EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE NORVEGIAE ET SUECIAE

VOL 55 | MARCH 1961 | FASC. 3

THE BLOOD VESSELS OF OSTEOGENIC SARCOMAS

Histologic, angiographic and microradiographic studies

by

CURT LAGERGREN, ÅKE LINDBOM and GUNNAR SÖDERBERG

It has long been known that some osteogenic sarcomas are highly vascular. The skin over such tumors is warmer than that covering the surrounding tissues and the subcutaneous veins are dilated. CODMAN has called this type of tumor a teleangiectatic osteogenic sarcoma. The high vascularity has been repeatedly demonstrated by means of angiography and when examined by this method most osteogenic sarcomas are found to be considerably richer in vessels than the surrounding normal tissues (BEGG, COLUMELLA & MUCCHI, FARINAS, FONTAINE et coll., STRICKLAND, SUTTON, TIWISINA, VOGLER & DEU). We have found, however, that some osteogenic sarcomas have *only a slightly* increased vascularity. VOGLER & DEU's material also included *three* bone sarcomas in which the number of vessels was not abnormally high. Since in recent years angiography has come to be used *to an* increasing extent as an aid in the diagnosis of bone tumors it was *considered* that a closer study of the vessels in these tumors might explain their variations in vascularity.

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Submitted for publication 22 September 1960.

Material. Twenty four cases of histologically confirmed osteogenic sarcomas were examined; angiography was performed in 21, none of which had previously received radiation therapy. In 13 of these cases, and in 3 others that had not been submitted to angiography, arteriography was performed on the amputation specimen. The vessels were examined both by combined microangiographic and histologic techniques described in an earlier report on the vessels of fibrosarcomas (LAGERGREN et coll.). A selection was made of parts of the tumor with different vascular structures as seen in the roentgenograms of decalcified sections, 0.5 cm thick, through the tumor. The degree of mineralization and the structure of the bony tissue of the tumor were studied by a microradiographic technique (ENGSTRÖM), representative areas being taken from undecalcified sections that had been embedded in methylmethacrylate and ground to a thickness of 100 to 200 microns. ENGFELDT, in his studies of the microradiographic structure of osteogenic sarcoma observed a wide variation in the appearance and degree of mineralization of the tumor bone.

Histologic findings

The tumors were classified according to the systems of JAFFE and DAHLIN. Three were labelled as juxtacortical osteogenic sarcoma, 12 as osteoblastic, 4 as chondroblastic and 5 as fibroblastic osteogenic sarcoma.

The vessels were readily identified in the histologic sections of the specimens containing contrast medium. There was a wide variation in the degree of bone formation in some of the osteoblastic sarcomas, some parts being as hard as cortical bone while others were not so firm and occasionally quite soft. Roentgenograms of a 0.5 cm thick section through such a tumor before and after decalcification are reproduced in Fig. 1. There was a soft, central extension of the growth into the medullary cavity of the diaphysis with a high cell density and little osteoid tissue and a low degree of differentiation to mineralized tumor bone. Many blood vessels in this part of the tumor had thin walls, resembling those of capillaries, with a single layer of endothelial cells or fibroblasts. The vessels had a pathologic irregular ramification and a wide variation in calibre (maximum 300 microns), some were sac like in form (Fig. 2, a and b), no elastic fibres were detected. This tumor structure in certain sections extended into the cortical layer, but it alternated with areas of moderate formation of osteoid tissue and a differentiation to irregular tumor bone. These areas contained fewer cells which were less irregular and presented fewer mitotic figures than the undifferentiated areas described above. The vessels were as a rule less abundant and more narrow (maximum calibre about 150 microns) and were seen to course in the spaces between the trabeculae of osteoid tissue and bone (Fig. 2, c and d). These vessels also contained no elastic fibres. A part of the tumor, of smooth contour and very hard consistency, protruded outside the corti



Fig 1 Roentgenograms of a 0 5 cm section of injected osteoblastic osteogenic sarcoma in distal metaphysis of the femur

a) Ordinary bone and bone forming tumor tissue intensively black Tumor occupies the medullary cavity and protrudes with bony part posteriorly outside cortex Microradiograms (see fig 3 c and d) were taken from adjacent sections in areas with same structure as those indicated by a cross

b) After decalcification Injected vessels are black indicating extension of hypervascularized tumor Heavily calcified parts are less vascular than the soft parts of the tumor in the medullary cavity F (a) Photomicrographs (see fig 2) and microangiograms (see fig 8) were taken from the areas indicated by arrows

cal bone (Fig 1) and contained a dense mesh of osteoid trabeculae with differentiation of mineralized tumor bone (Fig 2 e and f) The mineralization of the neoplastic bone was irregular The tumor bone trabeculae in some regions ran perpendicular to the cortical bone and in the relatively narrow spaces between the trabeculae small blood vessels of the capillary type (maximum calibre about 80 microns) were noted (Fig 2 e) There was no appreciable differentiation of the vessel walls in the tumor tissue but elastic fibres were observed in a few of the vessels The mineralization of the tumor bone was clearly defined with Heidenhain s staining method which is usually employed to demonstrate the striation of muscles the striations erythrocytes and mineralized bone appeared coal black while the osteoid tissue, with incomplete mineralization assumed different shades of grey (Fig 3 a and b)

Regions with as great a range of differentiation as found in this tumor were

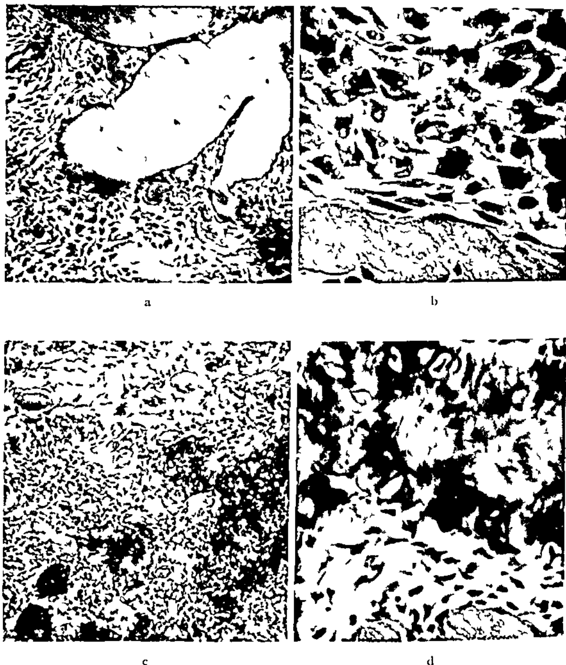


Fig 2 Photomicrographs of three different regions of the same osteogenic sarcoma as shown in fig 1 a) × 85 Poorly differentiated tumor extending into medullary cavity of diaphysis (upper arrow in fig 1 b) Dilated blood vessels containing contrast medium b) × 350 Higher magnification of (a) Anaplastic cells in non ossified part of tumor c) × 85 Intra osseous part (lower right arrow in fig 1b) with calcified osteoid and slightly dilated blood vessels d) × 350 Higher magnification of (c) Moderately atypical osteoblasts and osteoid

(For Fig 2 e and f see opposite page)



Fig 2 (e) × 85 Section highly differentiated part of tumor outside the cortex (lower left arrow in fig 1b) with capillary blood vessels between the bone trabeculae (f) × 350 High magnification of (e) Calcified osteoid and tumor osteoblasts with slightly to moderately atypical nuclei

(For Fig 2 a to d see opposite page)

distinguished also in several other tumors, but as a rule the difference between the areas was not so marked It was observed in several instances that vessels of a normal appearance penetrated a few millimetres into the peripheral part of the tumor tissue but further inwards they were destroyed and replaced by abnormal vessels

The same primary features were found in a juxtacortical osteogenic sarcoma of the distal metaphysis of the femur (Fig 4) The outermost layer in the parosteal region was surrounded by a zone of connective tissue that constituted a boundary between the tumor and the soft tissues A narrow zone of spindle cells with a moderate degree of nuclear and cellular polymorphism and fine streaks of osteoid tissue were evident beneath this layer There was more highly differentiated osteoid tissue and mineralized tumor bone organized into a dense trabecular framework below this in the major part of the parosteal region tumor tissue which was more cellular than polymorphous lay in the spaces of this framework The blood vessels were thin walled with occasional elastic fibres but with no distinct differentiation into arteries and veins they were of fairly small calibre and coursed in the spaces

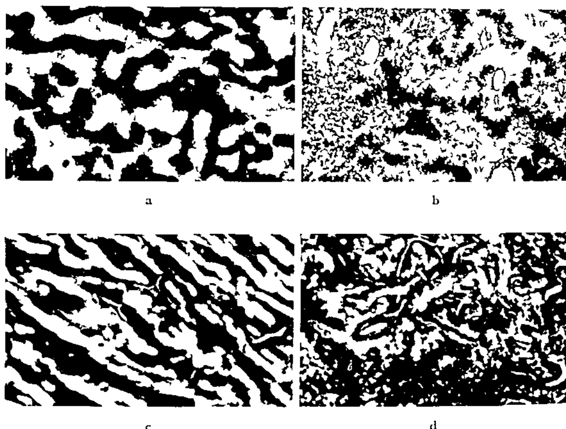


Fig. 3. Differentiation of neoplastic bone shown histologically and microradiographically. a) and b) Photomicrographs. Heidenhain's stain. × 35. Neoplastic bone trabeculae (black). a) Well differentiated part of tumor. b) Less differentiated part, trabeculae less mineralized, more irregular and sparse. c) and d) Microradiograms of approx. 100 micron sections. × 35. Bone trabeculae (white) the reverse of (a) and (b). Sharply defined white structures are vessels filled with contrast medium. c) Same part as in (a). Abnormal bone trabeculae, well differentiated. d) Same part as in (b). Abnormal bone trabeculae, poorly differentiated.

between the trabeculae of osteoid tissue and bone. An intermediate zone, which included the cortex and the subcortical region was present in this tumor; this contained a large quantity of osteoid tissue in the trabeculae, but the mineralization was considerably less marked here than in the parosteal part. Centrally in the metaphysis lay a poorly differentiated zone, probably proliferating as a secondary process into the spongy bone of the metaphysis, and composed of highly cellular tumor tissue with practically no osteoid tissue and only a few mineralized patches. The vessels in this zone were irregular, thin walled and wide (maximum calibre 300 microns) and much more numerous than elsewhere in the tumor. The cells were polymorphous, predominantly spindle shaped, with some of them stellate. Small areas of necrosis were also found in this zone.



F g 4 Juxtaco tical osteog nic sarcoma in typ cal locat on on popliteal su face of fem r) Arteriogram in si o Sl ght opacity of reg on in medullary cavity (arro s) b) *Decal fied 0.5 cm section of injected specimen (remnants of* calcium salt n cort cal laye s) Increased vascula ity cau es tumo to stand out dark aga nst u rounding bo e Part of tumor growing nto medullary cavity m e ascular than the est of it Cf mi oangiogram and microrad og ams in fig 9

Lobules of cartilaginous tissue with highly irregular cells were observed in two chondroblastic osteogenic sarcomas situated proximally in the tibia The blood vessels were situated in curved stretches of interlobular connective tissue Similar structures are found in a chondrosarcoma Areas of less dif ferentiated sarcoma tissue with spindle or polyhedral cells having irregular chromatin rich nuclei with islands of osteoid tissue and mineralized tumor bone and occasional irregular multinuclear giant cells were present in addi tion to the chondromatous lobuli The blood vessels in the connective tissue

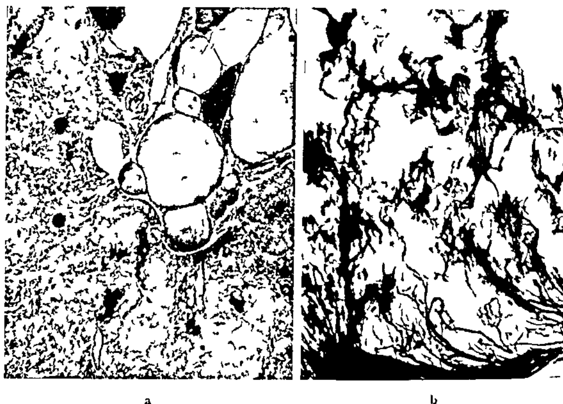


Fig 5 Vascular structure of chondroblastic osteogenic sarcoma a) Photomicrograph × 35 Large vessels filled with contrast medium between lobules of chondromatous neoplastic tissue b) Microangiogram × 12 Lobular pattern of condrosarcoma Wide curved interlobular vessels

between the lobuli were often very wide and thin walled (maximum calibre 500 microns) (Fig 5 a) The blood vessels in the cell rich and less differentiated parts of the tumor were more narrow and less regularly arranged and did not follow the curved course that was observed in the more highly differentiated cartilaginous parts

One fibroblastic osteogenic sarcoma, situated in the proximal metaphysis of the tibia, had a low degree of differentiation and little osteoid tissue This tumor contained highly irregular spindle cells with atypical chromatin rich nuclei and small amounts of fibrillar stroma The vessels were in parts very wide (maximum calibre 500 microns), the vessel walls were extremely thin, and the impression was gained that the tumor cells in some places actually constituted the wall of the vessels The vessels coursed circuitously but in a general direction, with convolutions and small irregular, sac like and bud like formations, they were densely spaced and in the main followed the general direction of the spindle cells of the tumor (Fig 6 a) Another fibroblastic osteogenic sarcoma of the distal metaphysis of the femur had similar features

Prior to the injection of the contrast medium, the amputation specimen

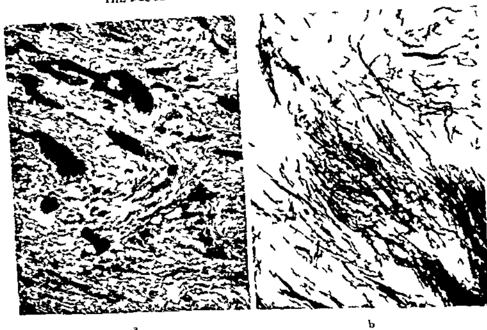


Fig 6 Vascular structure of fibroblastic osteogenic sarcoma a) Photomicrograph × 35 Mainly fibrosarcomatous tissue with many drawn out vessels filled with contrast medium arranged in the same general direction as the fibroblasts b) Microangiogram × 9 Streaky pattern sometimes also seen in well differentiated fibrosarcomas

was in a few cases perfused with normal saline containing glass spheres of various sizes (PRINZMETAL et coll) In one case of fibroblastic osteogenic sarcoma the venous efflux was found to contain glass spheres most of them up to 50 microns but some as large as 70 microns in diameter In the histologic sections many of the pearls were found caught in the tumor vessels and from this it may be inferred that there were shunts between the arteries and veins through the tumor these vessels had a diameter of 70 microns

Angiographic findings

Serial films were obtained in practically all the in vivo angiographic examinations An increase in the number of arteries around the tumor the presence of pathologic vessels within it (Fig 7) and an increase in the veins leaving the tumor area were noted The fact that these veins were filled with contrast medium earlier in the course of angiography than other veins in the surrounding tissues was regarded as evidence of shunting through the tumor The degree of vascularity of the tumors was estimated on the basis

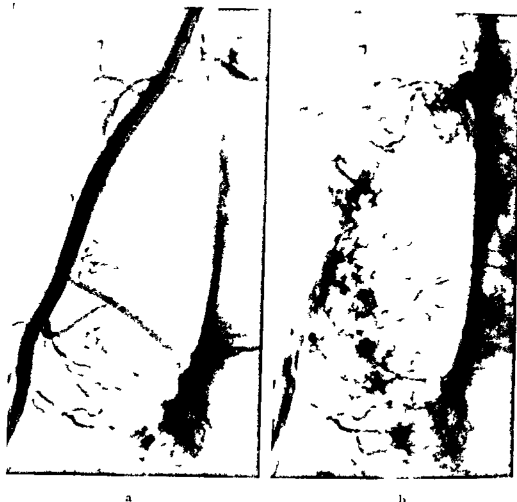


Fig 7 Pathologic tumor vessels in extra osseous part of osteoblastic osteogenic sarcoma in distal end of femur Serial angiography in vivo In early arterial phase (a) a few vessels filled with contrast medium two seconds later (b) typical dense network of pathologic vessels

of these findings In all cases the vascularity was greater in the tumor than in the surrounding tissues and ranged from moderate to marked

The extent to which the bone was destroyed or new bone was formed in each tumor was estimated in ordinary roentgenograms, the vascularity of the tumors was then compared with the degree of destruction and sclerosis The 13 cases presenting a high degree of vascularity all had destruction of bone, and in most of the tumors this tendency was more marked than the sclerosis, this was especially true in the more highly vascular cases The 8 cases in which the vascularity was moderate showed a more or less marked formation of bone, and this tendency was distinctly more evident than bone destruction Three tumors with no appreciable bone destruction had only slightly or moderately greater vascularity than the surrounding tissues



Fig 8 Vascularity in three different parts of same osteoblastic osteogenic sarcoma Microangiograms 9 of regions seen in figs 1 and 2 a) Well differentiated bony part Narrow parallel vessel b) Intermediate zone Wide more irregular vessels c) Poorly differentiated zone soft part Very wide irregular vessels

In 12 of the 21 cases there was a highly vascular soft part of the tumor *outside the* bone In several cases this contained thin streaks of tumor bone which were visible in the ordinary roentgenogram, although only in the angiogram was it possible to judge the size of this part of the tumor in some cases this part of the tumor did not contain bone and was visible only in the angiogram In 4 cases a highly vascular part of the tumor lay in the medullary cavity The boundary of the tumor in the latter could then be judged in the angiograms and in several cases it was found to have grown considerably more than was evident from the ordinary roentgenogram, as the cortical bone corresponding to this highly vascular part of the tumor was intact (See Fig 1)

The vascularity of the tumor in several cases in which the bone had not been penetrated was difficult to judge since in spite of satisfactory filling with contrast medium the vessels could not be distinguished through the often sclerosed bone The vessels were more easily demonstrated when higher kilovoltage and more concentrated (60 %) sodium diatrizoate was used

Microradiographic findings

It was evident from the microangiograms that all the tumors examined were at least in parts more highly vascular than the surrounding tissues Several of the osteoblastic tumors were markedly heterogeneous some regions

containing very dense wide vessels in an irregular reticular formation and others sparser, narrower, regular, and often parallel vessels (See Fig 1) The highly vascular areas corresponded in these tumors to the less differentiated areas where there was less new bone formation, while the sparser vessels were found in parts where there was considerable new bone (Fig 8) In one case of juxtacortical osteogenic sarcoma in the femur with an apparently secondary growth into the medullary cavity, the same difference between the various parts of the tumor was evident The part of the tumor outside the femur, in which the bone forming process was marked, thus contained more vessels than the normal cortical layer, they were, however, more regular and often more parallel than in the more highly and irregularly vascular and less differentiated parts of the tumor growing in the cavities of the spongy bone in the metaphysis (Fig 9, a and c) The vessels in the chondroblastic tumors followed a characteristic curved course between the cartilaginous lobules in the connective tissue and were often extremely wide and flattened (Fig 5 b) The microangiograms in the fibroblastic tumors showed bundles of wide parallel vessels winding around one another (Fig 6 b) These growths thus exhibited a different vascular structure from the osteoblastic tumors

The microradiographic examinations showed that the bony tissue of the tumors varied widely in its appearance and degree of mineralization, and that even when it was highly differentiated, the new bone differed from normal bone There were extremely few ordinary Haversian systems, and only traces of the regular lamellar structure of normal bone were found On the other hand, the fragments of residual normal bone which had not been destroyed by the tumor tissue presented the characteristic organization, with young, little mineralized and old, highly mineralized, Haversian systems

The highly differentiated parts of the sarcoma had a very regular appearance, with smooth uniform trabeculae with a high mineral content (Fig 9 b), in the sclerosed regions the trabeculae were often very densely arranged, more so than in normal spongy bone (Fig 9 b) The bone formed symmetric, long, parallel trabeculae in some of the highly differentiated areas (Fig 3 c)

The appearances were less uniform, with only a few large irregular trabeculae in the regions with a low degree of differentiation These trabeculae had a fairly high degree of mineralization and were surrounded by poorly, or sometimes only partly, mineralized trabeculae of varying thickness and direction (Fig 3 d) Where the degree of differentiation was still lower there was no evidence of trabeculae but irregularly dispersed patches with a varied but always low content of mineral salts were present, these patches sometimes merged to form a mossy network (Fig 9 d)

In some of the cases with an extra osseous tumor growth but with no tumor bone visible in the ordinary roentgenogram the microradiograms showed small mineralized regions with a varying degree of differentiation

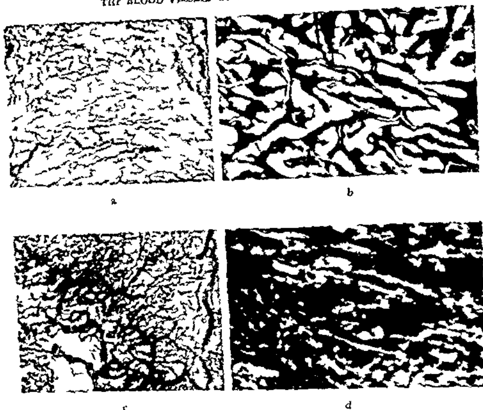


Fig. 9. Vascular and microradiographic structures of the juxta-cortical osteogenic sarcoma shown in fig. 4. a) Microangiogram × 9. Well differentiated part. b) Microradiogram × 35 of region similar to the one in (a). Coarse white structures are bone trabeculae and fine white streaks are vessels. Abnormal trabeculae dense and regular. c) Microangiogram × 9. Poorly differentiated part. d) Microradiogram × 35 of region similar to the one in (c). Abnormal trabeculae narrow and poorly mineralized.

Discussion

Most osteoblastic osteogenic sarcomas are very heterogenous tumors; that is to say, some parts of the tumor are highly differentiated with considerable new bone formation, whereas other parts are poorly differentiated with the formation only of osteoid tissue and little, if any, bone. In the parts of the tumor where the microradiograms showed a sparse, poorly organized formation of bone, the tumor tissue had a histologically more malignant appearance, with marked cellular irregularity and a high frequency of mitotic figures. Heidenhain staining revealed black structures very similar to the white structures in the microradiograms. There was a close agreement between the microradiographic and histologic structures of the different parts of the tumor

(Fig 3) The vessels in the poorly differentiated regions were extremely irregular and wide (cf Fig 2, a and b with Fig 8 c) In the regions where, on the other hand, fairly regular trabeculae were observed in the microradiograms and where the tumor tissue was histologically less malignant, the vessels were narrower and more regular (cf Fig 2, e and f with Fig 8 a), a few elastic fibres could be seen in the vessel walls, which suggested some degree of differentiation also of the vessels In an earlier paper on fibrosarcomas we have presented evidence of a relationship between the vascularity and the degree of malignancy in these tumors The same conclusion seems to apply to the osteogenic sarcomas The less differentiated parts of these tumors with little new bone formation are much more vascular than the more highly differentiated parts where there is massive bone formation and where the vascularity is not much greater than in the normal tissue

On angiography the juxtacortical osteogenic sarcoma with considerable new bone formation presented only a moderately increased vascularity in relation to the surrounding tissues These highly differentiated tumors have probably as a rule no poorly differentiated malignant and vascular components, which possibly explains their considerably more benign nature compared to the ordinary osteogenic sarcoma JAFFE distinguishes two types of juxtacortical osteogenic sarcoma, one of which has a more malignant course When angiography reveals a highly vascular region in such a tumor, it is probably of the more malignant type (see Fig 4)

Angiography in most of the ordinary heterogeneous osteoblastic osteogenic sarcomas revealed highly vascular parts from which cells or cell aggregates might more easily be carried away to the lungs than from the less richly vascular parts The angiographic demonstration of these highly vascular parts of the tumor constitutes a valuable support for the diagnosis

A histologic diagnosis is generally desirable in these cases, especially when amputation is intended A soft tumor component growing out from the bone can often be demonstrated angiographically, and in such cases it is best to take a biopsy specimen from this region in order to obtain as early a diagnosis as possible (Fig 7) In some cases the angiograms will indicate how far the tumor has grown into the medullary cavity A difference in the microangiographic structure of the various types of osteogenic sarcoma can be demonstrated The chondroblastic parts of the tumor have a lobular structure which has commonly been observed in the chondrosarcoma, the fibroblastic tumors have a streaky structure, which has been observed in some previous cases of fibrosarcomas It is thus possible, in some cases at least, to recognize the various tumor tissues by their microangiographic structure (cf Figs 5 b, 6 b and 8) In the ordinary in vivo angiographic examinations however, only the coarser vascular structures will be visible so that it is uncertain whether the various types of tumor can be distinguished with the present angiographic techniques

The following conclusions may be drawn with respect to the angiographic diagnosis

The juxtacortical osteogenic sarcoma is only slightly more vascular than the surrounding tissue With a secondary growth into the marrow space the tumor may be highly vascular

An osteoblastic osteogenic sarcoma usually contains highly vascular parts which can be demonstrated in the angiogram this feature provides a valuable confirmation of the diagnosis

A few osteoblastic osteogenic sarcomas which display little tendency to osteolysis are only slightly more vascular than the surrounding tissue

It is probable that fibroblastic and chondroblastic osteogenic sarcomas are as a rule highly vascular

SUMMARY

Twenty four cases of osteogenic sarcoma were examined The vascularity of the osteoblastic form of these tumors varied with the degree of malignancy Most but not all of the tumors contained very malignant highly vascular parts which could be demonstrated angiographically and which provided confirmation of the diagnosis Different forms of osteogenic sarcoma were found to display microangiographic differences in structure

ZUSAMMENFASSUNG

Vierundzwanzig Fälle von osteogenem Sarkom wurden untersucht Die Vaskularisation des osteoblastischen Typus dieser Tumoren variierte mit dem Grad der Malignität Die meisten Tumore doch nicht alle enthielten hochmaligne stark vaskularisierte Partien die angiographisch demonstriert werden konnten und die Diagnose bestärkten Es wurde gefunden, dass verschiedene Formen von osteogenen Sarkomen eine verschiedene mikroangiographische Struktur haben

RÉSUMÉ

Les auteurs ont examiné vingt-quatre cas de sarcome osteogénique Le caractere vasculaire de la forme osteoblastique de ces tumeurs varie suivant le degré de malignité La plupart, mais non la totalité de ces tumeurs comprenait des parties tres malignes hautement vasculaires qui ont pu etre mises en évidence par l angiographie et qui ont apporte une confirmation au diagnostic Les auteurs ont constaté que des formes différentes de sarcomes ostéogeniques présentent des differences microangiographiques de structure

REFERENCES

BEGG A C The vascular pattern as an aid to the diagnosis of bone tumours J Bone Jt Surg 37 B (1955) 371

COLUMELLA F e MUCCHI L Biopsia o arteriografia nella diagnostica delle osteopatie degli a ti Chirurgia (Milano) 8 (1953) 311

DAHLIN D C Bone tumors General aspects and an analysis of 2 276 cases Charles C Thomas Springfield Ill 1957

ENGFELDT B Biophysical studies on bone tissue VI Biophysical studies on bone tissue from osteogenic sarcoma Cancer 7 (1954) 815

ENGSTRÖM A X ray microscopy *In* Analytical cytology Chapter V second edition p 343 Edit Robert Charles Mellors McGraw Hill New York 1959

FARINAS P L Diagnosis of bone tumors of extremities by arteriography Radiology 29 (1937) 29

FONTAINE, R WALTER P, KIM M et KIENY R De l utilite de l arteriographie pour le diagnostic des tumeurs des membres d origine osseuse et extra osseuse J Radiol Electrol 35 (1954) 165

JAFFE H L Tumors and tumorous conditions of the bones and joints Lea & Febiger Philadelphia 1958

LAGERGREN C LINDBOM A and SODERBERG G Vascularization of fibromatous and fibro sarcomatous tumors Acta radiol 53 (1960) 1

PRINZMETAL M ORNITZ Jr E M SIMKIN B and BERGMAN H C Arterio venous anastomoses in liver spleen and lungs Amer J Physiol 152 (1948) 48

STRICKLAND B The value of arteriography in the diagnosis of bone tumours Brit J Radiol 32 (1959) 705

SUTTON D Percutaneous angiography with special reference to peripheral vessels Brit J Radiol 28 (1955) 13

THEISINA H Angiografische Studien bei bosartigen Geschwulsten der Gliedmasen Fortschr Rontgenstr 87 (1957) 206

VOGLER E und DIEL W Der Wert der Angiographie in den Tumordiagnostik der Extremitaten Fortschr Rontgenstr 83 (1955) 158

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MEDIONECROTIC DISSECTING ANEURYSM OF THE ABDOMINAL AORTA

Report of a case diagnosed by means of aortography

by

HANS LUDIN PETER WAIBEL and SIEGFRIED SCHEIDEGGER

Dissection of the walls of the aorta or peripheral arteries may result from arteriosclerosis medionecrosis or trauma such as the intramural injection of contrast media in lumbar aortography (WOLFMAN and BOBLITT)

Medionecrosis of the aorta occurs much less often than arteriosclerosis but when it exists frequently causes dissection Its primary site of predilection is the ascending aorta Dissecting medionecrosis confined to the abdominal aorta and its ramifications is so rare that KNUTSSON (1959) wrote Medionecrosis aortae idiopathica does not appear in the abdominal aorta We have however had the opportunity of establishing the diagnosis of such a condition by aortography prior to operation and ante mortem and feel justified in reporting our case in detail

A woman aged 66 with no significant history apart from slight systolic hypertension of 160 mm Hg and some dyspnoea on exertion suddenly experienced severe lumbar pain radiating over the abdomen the symptoms gradually subsided The next day similar pain but of increasing severity caused her to collapse the pain then gradually subsided Four days later following a further attack she was admitted to hospital On examination her blood pressure was 55/25 she was somnolent and in poor general condition There was no abdominal rigidity the legs were somewhat oedematous but not cyanosed Following blood transfusion the blood pressure rose to 165/95 and a strong right sided paravertebral pulsation

Submitted for publication 19 September 1960



Fig 1 Retrograde aortograms in supine and right posterior oblique positions The dissection channel is projected to the left of the aortic outline

could be felt on abdominal palpation Despite numerous transfusions the haematocrit values dropped continuously yet only a trace of occult blood was present in the faeces A tentative clinical diagnosis of retroperitoneal haemorrhage from an abdominal aortic aneurysm was made

On retrograde aortography it proved impossible to pass the catheter up through the upper part of the right or left iliac arteries 40 ml Urografin 76 % were therefore injected under high pressure and after compressing both femoral arteries with the tip of the catheter placed near the origin of the left hypogastric artery The patient collapsed repeatedly during this procedure and was treated with further transfusions Apparently because of the low blood pressure the contrast medium could be forced up the abdominal aorta to the level of the renal arteries The same quantity of contrast medium was again injected with the patient in the left posterior oblique position

The examination showed (Fig 1) marked displacement of a dilated portion of the abdominal aorta to the right up to the level of L 1—L 2 a few centimeters below the origin

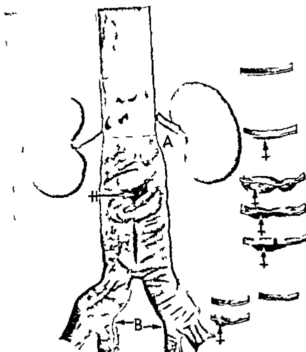


Fig 2 Autopsy specimen open d from behind The ves els are widened betw n (A) and (B) The dissection chann l (‡) is indi cated at the cross sections seen to the right these correspond to the va ious levels of the aort c wall indicated by striped lines. Transverse ruptures of the inner layers of the aortic wall (↔)

f the renal arteries which were not filled The aortic segment above the abruptly ending dilatation had except for its S-shaped connection with the aneurysm a normal left para sagittal position a normal calibre and smooth contours The aortic bifurcation was displaced to the right and posteriorly Whereas the contours of the dilated portion of the abdominal aorta were quite smooth on the right side a 7 to 8 cm wide dissection channel was visible in front of and slightly to the left of the aortic lumen reaching from the vicinity of the upper lim t of the d latation down to the left common iliac artery just proximal to the origin of the left hypogastric artery The velocity of flow within the dissection channel and the main vessel was about equal Additional films obtained after a few minutes revealed a left para vertebral retroperitoneal contrast extravasate which displaced the left psoas muscle and ureter laterally The diagnosis of a dissecting aneurysm of the abdominal aorta with retroperitoneal bleeding was established Better knowledge of the pathology of dissecting aneurysms would probably have permitted the diagnosis of medionecrosis to have been made from the smooth ness of the aneurysmal walls and the normal appearance of the upper portion of the ab dominal aorta and the lower iliac and femoral arteries

A few hours later an anterior external rupture of the aorta was sutured The patient re covered satisfactorily after the operation and further transfusions Nine days after operation a slight icteric discoloration and a moderate azotaemia appeared diminishing however



Fig. 1. Retrograde aortograms in supine and right posterior oblique positions. The dissection channel is projected to the left of the aortic outline.

could be felt on abdominal palpation. Despite numerous transfusions the haematocrit values dropped continuously, yet only a trace of occult blood was present in the faeces. A tentative clinical diagnosis of retroperitoneal haemorrhage from an abdominal aortic aneurysm was made.

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Discussion

Dissection of the arterial wall in arteriosclerosis mostly quite limited in extent is caused by ulceration of the intima and media *Atherosclerosis with* complicating aneurysmal dilatation and dissection is a disease affecting older *age groups* Among 15 autopsy cases of dissecting aneurysms reported by LODWICK, 12 were of the arteriosclerotic type mostly situated in the lower abdominal aorta and most of them asymptomatic *The average age was over 70 years*

Medionecrotic dissecting aneurysms, however, occur far less frequently According to SAILER they are detected in about 0 25 per cent of autopsy cases, wherea MANIGLIA and GREGORY have found *arteriosclerotic aortic aneurysms in one pe cent* of 1 000 autopsies, 80 per cent of these aneurysms being situated in the abdominal aorta SHENNAN states that most medionecrotic aneurysms occur between the fourth and the seventh decades The average age of three cases reported by *LODWICK was 33 years According to* SHENNAN medionecrosis occurs not infrequently at younger ages and even in infancy The primary lesion is situated almost exclusively in the ascending aorta and the aortic arch The aneurysms often dissect into the brachiocephalic arteries and in about 40 per cent of cases down into the lumbar aorta or even into the iliac arteries (MOTE and CARR) In one case described by LODWICK three separate dissected portions situated in the proximal and distal part of the aortic arch and below *the origin of the renal arteries were found* SHENNAN reported dissections to be multiple in about 10 per cent of cases

KAUFMANN describes the autopsy findings in a young female with annular dissection of the lumbar aorta extending down to the iliac arteries and fatal haemorrhage due to external rupture Histologic findings are not reported, but the young age suggests the lesion to have been of the medionecrotic type One case reported by JOHNS showed much similarity to ours the internal *rupture was situated just below the inferior* mesenteric artery and the external perforation slightly below the inner one The external perforation was sutured but the patient died on the eighth postoperative day because of renal failure due to nephrosis Autopsy revealed the lesion to be of the medionecrotic type, an exact preoperative diagnosis was *not* established

It appears that the cases described by DE ANGELIS STAEMMLER SZILAGYI and EYLER were of an arteriosclerotic nature The only case in which a pre operative *aortographic diagnosis of* the condition has been established seems to be the one reported by EYLER probably identical with *the one discussed* by SZILAGYI in which the aneurysm was resected and successfully replaced by *a graft* Further cases have not been found in the literature

The aetiology and pathogenesis of *medionecrotic* aneurysms is not well understood for it is not clear whether the rupture of the intima and the adjacent inner two-thirds of the media originates from the lumen or from the layer

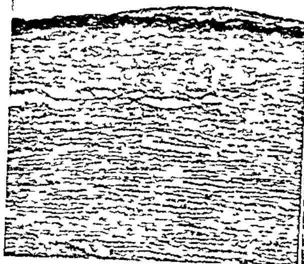


Fig 3 *Idiopathic* medionecrosis of the aorta Numerous cystic spaces of the *media with mucoid* degeneration

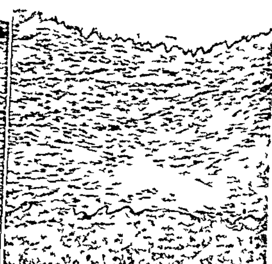


Fig 4 Large cystic space in the media with mucoid degeneration and diffuse fibrosis in media and adventitia

during the following days These signs increased again two weeks after operation, and the urine contained some casts indicating kidney damage Some days later another attack of shock and collapse occurred and a haemorrhagic diathesis developed After an attempt at treatment by dialysis the patient died with pulmonary oedema on the nineteenth day after operation

Autopsy confirmed the radiologic findings Fig 2 is a drawing of the aorta opened from behind and the findings at cross sections through the aorta and iliac arteries at various levels The sudden increase of the aortic circumference by 2 5 cm about two centimeters below the origin of the renal arteries is clearly demonstrated (arrow A) the widened portion reaches down to the common iliac arteries (arrow B) The dissection channel extends from the upper end of the aneurysm down to the lower extremity of the diseased vascular segment in the left common iliac artery (see cross sections ↔) The involved vessels had lost their normal resilience some slight and localized atheromatous changes were found within the thoracic aorta The first transverse rupture of the inner layers of the aortic wall proved histologically to be quite recent and may have occurred when the first symptoms appeared The complete external rupture of the aortic wall measuring 3 3 cm in length was partially closed by sutures The wall had apparently ruptured beyond the sutured area during the last attack of collapse and shock Histologic examination suggested the complete rupture to be more recent than the inner rupture

The retroperitoneal and pelvic connective tissue was infiltrated by relatively fresh blood Both renal arteries were intact The small and large bowel showed extensive haemorrhagic infarctions with slight paralytic ileus evidently due to partial occlusion of the mesenteric arteries caused by the aortic dissection

Histologic examination of the wall of the diseased portion of the abdominal aorta and common iliac arteries revealed the presence of a typical medionecrosis usually to be found in cases of dissecting aneurysms of the aortic arch The atheromatous changes and fibrosis of the intimal layer appeared less in degree and extent than usually seen in cases of the same age and sex A new intima had not yet formed in the dissection channel situated within the necrotic media (Figs 3 and 4) A few vasa vasorum showed a *moderate proliferation* of the intima and some small round cell infiltration of the adventitia

This hypothesis explains the observation of LODWICK in one of his cases of a medionecrotic type in which cyanosis and ischaemia of the lower part of the body disappeared immediately as soon as re entry took place Thus the establishment of a re entry prevents external perforation and progress of dissection not by lowering the blood pressure within the dissection channel D, but by *stabilizing the status quo* In arteriosclerosis the inner flap will be more rigid and the media more effective at resisting dissection than in medionecrosis, thus explaining the lesser extent of dissection *in the former condition*

Symptoms are caused by partial or total obliteration of the lumen of the aorta (see above), of its branches by *compressing* their origin (spinal cord and cerebral ischaemia haemorrhagic infarction of the intestines, renal damage), but mainly by acute or subacute massive haemorrhage due to external perforation According to the location and severity of the haemorrhage the main lesion will be situated in the central nervous system (cerebral ischaemia) the pericardium (cardiac tamponade, coronary insufficiency), or the kidneys (shock kidneys)

Death follows the onset of symptoms at greatly varying intervals depending on the above factors (JONES and LANGLEY SHENNAN)

In the surgical treatment the following techniques are employed

1 Resection and grafting resulting when feasible and successful in permanent cure

2 Suture of the primary intimal tear in cases without re entry The tear is often very difficult to locate even at autopsy (SHENNAN WARREN BECKWITH and MULLER)

3 Fenestration (DE BAKEY) in cases without re entry (see above)

4 Reinforcement of the aortic wall by covering it with orlon tissue (WARREN BECKWITH and MULLER)

5 Fenestration combined with resection and grafting of the aortic portion distal to the fenestration (WARREN BECKWITH and MULLER)

6 Suture of the external rupture — merely symptomatic treatment.

Operative results depend on the location and nature of the lesion and the procedure employed In DE BAKEY s material there were 7 survivors out of 10 patients whereas WARREN BECKWITH and MULLER reported only one survivor out of 5 patients Recurrent bleeding and renal failure seem to be the most important causes of *postoperative death* *Lesions* of the abdominal aorta probably have a better prognosis than those involving the aortic arch they do not cause cardiac tamponade and are *easier to detect clinically and radiologically* from unexplained blood loss lumbar pain abdominal signs and lateral displacement of the psoas muscle and ureter The dilated aortic *portion can often be palpated* The abdominal aorta may b clamped off distal to the renal arteries for a period sufficient to permit resection and grafting *which* is evidently the ideal *procedure*

Diagnostic radiology can contribute important information for the evaluation of the local pathology underlying the clinical picture *it can also afford* confirmation of the diagnosis of retroperitoneal haemorrhage and angiographic demonstration of the *nature and* extent of the lesion Injection of contrast medium well above the proximal end of the aneurysm will demonstrate or

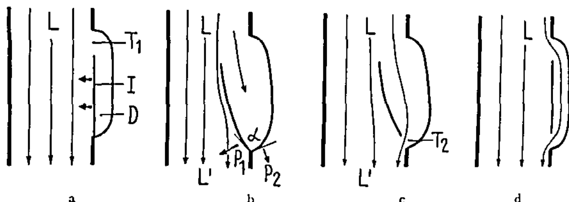


Fig. 5. Pathogenesis of extension of aortic wall dissection. D — Dissection channel. I — Flap. L — Aortic lumen above flap. L' — Aortic lumen below flap. P_1 and P_2 — Blood pressure components. T_1 — Primary transverse tear. T_2 — Secondary transverse tear.

in which dissection takes place. According to the latter hypothesis (KRUKENBERG, SAILER, KAUFMANN) a mural haematoma would first develop, probably from some lesion of the vasa vasorum. Repeated paroxysmal extension of the dissection may be explained as follows.

Blood entering the dissection channel D (Fig. 5) from the aortic lumen L through a transverse tear T_1 mobilizes an inner flap I. Blood flowing within L will exert a systolic pull of about 2 to 3 g/cm² and a diastolic pull of about 0.5 g/cm² on the flap, as calculated from Bernoulli's formula, the pull being a quadratic function of blood velocity. It remains speculative whether turbulence will occur, but probably some additional haemodynamic pressure, due to the prominence of the flap into the lumen, will enhance the oscillatory central displacement of the flap, depending on flap mobility, blood flow, and the aortic dimension. It appears questionable whether such forces are sufficient to produce slow extension of the dissection. Increased blood flow, however, due to physical exertion etc., may cause the flap to move towards the opposite aortic wall to such an extent that blood flow along the flap is markedly diminished, and blood pressure below the flap in L' is lowered. This causes the flap to be pressed towards the opposite wall, blocking the blood flow. The entire aortic blood pressure is exerted on the walls of the dissection channel D, thus also on its distal extremity with components P_1 and P_2 at an angle of 180° — α, producing a sudden and rapidly progressive distal dissection, mostly followed by re-entry or external rupture according to the local pathology. This explains why intercostal and lumbar arteries are not infrequently torn across. When a re-entry T_2 is established, either spontaneously or by operative fenestration (DE BAKEY), rising blood pressure in L' causes the flap to move back (Fig. 5 c) and blood will then flow through L and D (Fig. 5 d), the blood pressure being about equal in both lumina.

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preclude the presence of an open dissection channel and exclude the possibility of an abdominal extension of a thoracic dissection Even a closed dissection channel may be detectable if the aorta shows a markedly unequal diameter in lateral or oblique views or if the aortic wall is rather smooth or the upper limit of the narrow portion is abrupt Irregularity of the outline of adjacent vessels would rather suggest an arteriosclerotic basis It is evident that high retrograde aortography, when feasible, is the procedure of choice provided the catheterisation is performed very carefully

Acknowledgement

We wish to thank Prof H Heusser Director of the Second Surgical Department of Basle University Hospital and his co workers for referring the patient and for the clinical records

SUMMARY

A case of medionecrotic dissecting aneurysm of the abdominal aorta has been diagnosed by means of retrograde percutaneous aortography The possibilities of angiographic diagnosis the differences between arteriosclerotic and medionecrotic dissecting aneurysms, the symptomatology and therapeutic procedures together with an hypothesis on the mechanics of the extension of dissections, are discussed

ZUSAMMENFASSUNG

Ein Fall von medionekrotischem dissezierendem Aneurysma der Abdominalaorta wurde mittels retrograder perkutaner Aortographie diagnostiziert Die Moglichkeiten der angiographischen Diagnosestellung die Unterschiede zwischen arteriosklerotischen und medionekrotischen dissezierenden Aneurysmen die Symptomatologie und Therapie sowie eine Hypothese uber die Mechanik der Ausbreitung der dissezierenden Veranderungen werden besprochen

RÉSUMÉ

Un cas d anévrisme disséquant par nécrose de la media de l aorte abdominale a été diagnostiqué par aortographie retrograde percutanée Les auteurs étudient les possibilités du diagnostic angiographique les différences entre les anévrismes disséquants artérioscléreux et medionécrotique la symptomatologie et les traitements ainsi qu une hypothese sur le mécanisme de l extension du processus disséquant

REFERENCES

De Angelis E Dissecting aneurysm of the abdominal aorta Amer Heart J 26 (1943) 124
De Bakey M E Cooley D A and Creech Jr O Surgical considerations of dissecting aneurysm of the aorta Ann Surg 142 (1955) 586
Eyler W R Lumbar and peripheral arteriography technics and radiologic anatomy Radiology 69 (1957) 165
Johns T N P Dissecting aneurysm of the abdominal aorta Ann Surg 137 (1953) 232
Jones A M and Langley F A Chronic dissecting aneurysms Brit Heart J 8 (1946) 191
Kaufmann F Lehrbuch der speziellen pathologischen Anatomie 7 und 8 Aufl Walter De Gruyter Berlin 1928

KNUTSSON F Dissecting aneurysm of the thoracic aorta Acta radiol 51 (1959) 273

KRUKENBERG E Beitrage zur Frage des Aneurysma dissecans Zieglers Beitr 67 (1920) 329

LODWICK G S Dissecting aneurysms of the thoracic and abdominal aorta — report of six cases with a discussion of roentgenologic findings and pathologic changes Amer J Roentgenol 69 (1953) 907

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FROM THE DEPARTMENT OF NEURORADIOLOGY (DIRECTOR H H JACOBSEN), RIGSHOSPITALET, COPENHAGEN, DENMARK

PANTOPAQUE MYELOGRAPHY IN AVULSION OF THE BRACHIAL PLEXUS

by

JACK LESTER

A tearing away of the nerve roots from the medulla spinalis in the brachial plexus produces a clinical picture which, although characteristic, cannot definitely be distinguished without the aid of myelography from more peripheral lesions of the corresponding nerve roots Typical myelographic appearances in these lesions were first described in 1947 by MURPHEY, HARTUNG, and KIRKLIN who, by 1949, had encountered 7 cases In 1954, WHITLEATHER of the same clinic reported 8 cases, 4 of which had, however, already been mentioned in 1949 Similar cases have been published by JAEGER and WHITELEY (1953), TARLOV and DAY (1954), WHITE and HANELIN (1954), RASLE et coll (1955), WIEDENMANN and DECKER (1956), BORELLI and MAGLIONE (1956), SASSAROLI and SPACCARELLI (1957), PASSARINI (1959), and RASMUSSEN (1959) In all, 33 cases of brachial plexus avulsion diagnosed by pantopaque myelography have been reported, 12 of these have been confirmed at operation

These avulsions arise as a result of severe injury to the shoulder region, usually after a motor accident or a fall from a height Multiple fractures and sometimes cranial trauma with loss of consciousness are often present as well In lesion of the uppermost roots (C5, to C7) Erb Duchenne paralysis, affecting mainly the shoulder movements and elbow flexion, may occur Damage of the lower roots (C8 and Th1) produces Klumpke s paralysis, which chiefly involves the muscles of the hand If Th1 has been torn away Horner's syndrome is also evident, owing to injury of the sympathetic fibres to the stellate ganglion

Submitted for publication 14 July 1960

Flaccid paralysis with corresponding impairment of the sensory function usually sets in at once as the sensory nerve roots are thicker and hence have greater powers of resistance than the motor roots (TARLOV) the sensory impairment may however be less extensive Burning or darting pain along the affected nerve pathways is often reported

A tentative diagnosis may be made by spinal puncture the cerebrospinal fluid usually being blood streaked during the first 5 to 6 weeks Electro myography is another important aid in indicating the extent of the damage

Exact clinical localization of the nerve damage is often difficult owing to masking by injuries of the soft tissue and bone However, a lesion of the dorsal scapular and long thoracic nerves (paresis of the rhomboideus, levator scapulae, and serratus anterior muscles) and a lesion of the sympathetic fibres in Th1 (Horner s syndrome) indicate that the nerves have been damaged either before or directly after their emergence from the intervertebral foramina, and hence suggest that avulsion has occurred Signs of injury to the medulla spinalis also point to the same possibility (JAEGER and WHITELEY)

As a result of violent trauma the dura mater and the arachnoidea which en circle the roots as far as the foramina may become torn The dura mater is the stronger of the two membranes, while the arachnoid membrane and the slender radicular fibres are easily damaged following damage to the former, the cerebrospinal fluid then leaks out into the space formed when the pe ripheral nerve stump retracts The dura and arachnoidea gradually proliferate and close this space to produce a kind of traumatic meningocele (WHITE and HANELIN) a feature underlying the characteristic myelographic appearances

Myelography with iodized oil (Pantopaque) reveals in typical cases that the contrast medium runs outside the vertebral canal towards the inter vertebral foramina and collects in diverticulum like pockets corresponding to the avulsed roots The myelographic examination should be carried out with the patient in the prone position when the opening of the pockets lies at the lowest level At least 6 preferably 9 ml of contrast medium should be used as filling of the pockets takes some time and may fail to occur if too small an amount of medium passes too rapidly WHITE and HANELIN for instance observed defective filling of a pocket in one of their cases and found ob structing adhesions at subsequent exploration

The avulsions may have two different myelographic appearances but both are often seen in one and the same case (1) contrast filled extradural pockets ranging in size from a pea to a walnut and extending obliquely and caudally from the vertebral canal to the foramina (Figs 1 2 and 3) (2) less marked changes in the lateral outline of the contrast medium at the site of the affected spinal nerves The outline may either be convex medially (TARLOV) irregular and wavy (BORELLI) or as we have observed in several cases show a slight bulge with the convexity laterally In all cases absence of the usual rounded defect in the contrast filling at the exit site of the spinal nerves is a charac



Fig 1 Case 1 Typical large Pantopaque filled avulsion pocket at the level of the left C 8 and a slightly smaller pocket at Th 1



Fig 2 Case 2 Typical avulsion pocket at left C 7 Small bulge and laterally directed convexity at level of C 6 Normal root outlines absent asymmetry



Fig 3 Case 3 Large avulsion pocket at the site of left C 6 Irregular defect in contrast out line at C 7 probably indicating lesion of the medulla spinalis and absence of the normal defect corresponding to the nerve root

teristic feature A comparison with the sound side shows the condition to be asymmetric (Figs 4 and 5)

Roentgen appearances resembling an avulsion are seen only in the rare extradural arachnoid cysts These are, however, most commonly found in the thoracic region in association with Scheuermann s disease (Good et coll 1944), they have been observed in the cervical region in only 3 cases (Meredith 1940 Pendergrass et coll 1956, and Rayle et coll) Differential diagnostic problems can hardly arise, however, because the anamnesis and the absence of relevant neurologic signs and symptoms exclude an avulsion

The prognosis is obviously poor in these avulsions No appreciable regression, either spontaneous or following a neurosurgical operation, can be expected The most suitable form of treatment is physiotherapy, movement therapy to keep the joints mobile and myotensor treatment to maintain muscle function Orthopaedic intervention, or amputation, may have to be undertaken at a later stage

Material

We have established with the aid of pantopaque myelography the presence of one or more avulsions in 6 patients within the course of six months These consisted of 5 men and one woman ranging in age from 19 to 39 years In 5 of the cases the condition was the result of a motor accident while the sixth patient with a fractured scapula had caught his arm in a winch on a fishing boat Five of the 6 patients had various other fractures and 3 had had a head injury with loss of consciousness Pantopaque myelography was undertaken

in these 6 cases 14 days to 5 months after the accident In 3 patients who were examined two two and a half, and six weeks respectively after the injury slightly blood streaked cerebrospinal fluid was present, in the others, includ ing one patient examined 18 days after the accident the fluid was clear

Clinically 2 patients had Erb Duchenne paralysis avulsion of C 5 and C 6 was demonstrated in one of them and of C 6 and C 7 in the other The former had paresis of the diaphragm as well this was not observed in any of the other patients In 3 patients with Klumpke s paralysis and Horner s syndrome avulsion of C 8 and Th 1 was noted The sixth patient had completely flaccid paralysis of one arm and Horner s syndrome myelography revealed avulsion of C 7 and C 8, and Th 1

After the diagnosis had been established by myelography none of the patients were submitted to operation but were advised to undergo physiotherapy or *orthopaedic treatment*

Case reports

Case 1 Male aged 24 with paresis of both arms and the left leg immediately after a motor accident Contusion of the medulla spinalis and fracture of the third thoracic vertebra were diagnosed at another hospital Regression of the paresis of the right arm and left leg soon occurred but the left arm did not improve Six months after the trauma he had left-sided miosis slight diffuse weakness of the right arm and left leg and severe paresis of the left arm with dystrophy of the hand Pantopaque myelography (clear spinal fluid) revealed a large typical avulsion pocket filled with contrast medium at the left C 8 and a smaller pocket at the level of Th 1 (Fig 1) Roentgen diagnosis Avulsion of C 8 and Th 1 on the left side

Case 2 Male aged 19 with paresis of the shoulder and elbow immediately after a motor cycle accident involving trauma to the left shoulder One month later he had total paralysis of the deltoid and pectoralis muscles with anaesthesia and analgesia of the corresponding areas atrophy of the left deltoid and infraspinatus muscles as well as of the muscles of the upper arm was also noted As suboccipital air myelography (slightly blood streaked spinal fluid) suggested avulsion of the left C 7 pantopaque myelography was performed and revealed a typical avulsion cyst at this site A small bulge in the contrast outline with the convexity laterally was visible at the level of C 6 and at the same time the normal outline of the root was absent in other words there was definite asymmetry as compared with the right side (Fig 2) Roentgen diagnosis Avulsion of the left C 6 and C 7

Case 3 Female aged 39 had been admitted to another hospital after a motorcycle accident involving loss of consciousness for a few minutes followed by severe paresis of the left arm She also had fractures of the left transverse processes of the seventh cervical and first thoracic vertebrae A fortnight later paralysis of the shoulder movements severe paresis of the ex tension and flexion movements of the elbow and partial paresis of the hand muscles persisted on the left side as well as analgesia on the dorsal aspect of the left shoulder Roentgen ex amination of the thorax revealed that the left side of the diaphragm was raised Myelography (clear spinal fluid) showed a large avulsion pocket at the site of the left C 6 a large irregular defect in the contrast filling was seen at the level of C 7 and the normal contrast defect corresponding to the nerve root was not visible (Fig 3) Roentgen diagnosis Avulsion of the roots of C 6 and C 7 on the left side with probable lesion of the medulla spinalis at C 7



Fig 4 Case 5 Small bulges in the contrast outline and no signs of root contours at the right C 8 and Th 1 (Cf normal root contours on left side)

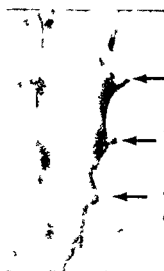


Fig 5 Case 6 Small lateral projections from the contrast outline and no signs of root contours at level of the left C 7 C 8 and Th 1



Fig 6 Extradural arachnoidal cyst in a man aged 53 without clinical signs of avulsion Small contrast filled pocket at the right C 8 but directly above it the defect corresponding to the nerve root is intact

Case 4 Male aged 28 had caught his right arm in the winch of a fishing boat resulting in fracture of the neck of the scapula When admitted 8 days later flaccid paralysis of the right upper arm and Horner s syndrome were noted Suboccipital air myelography (slightly blood streaked spinal fluid) suggested an air filled avulsion cyst at the site of the right C 8 and pantopaque myelography revealed a large typical avulsion pocket at the right C 8 and absence of a contrast defect at the root of Th 1 Roentgen diagnosis Avulsion of the right C 8 and Th 1

Case 5 Male aged 24 who was admitted with a fracture of the lower jaw and paralysis *of the right arm following a motorcycle accident One month later he had paralysis* of the right lower arm and hand with areflexia anaesthesia of the lower part of the arm and Horner s syndrome Myelography (clear spinal fluid) revealed small bulges in the contrast outline and absence of the root contours at the level of the right C 8 and Th 1 (Fig 4) Roentgen diagnosis Avulsion of the right C 8 and Th 1

Case 6 Male aged 22 admitted after a motorcycle accident involving loss of consciousness and fracture of the left lower arm with diffuse paresis and corresponding anaesthesia and analgesia of the entire left arm and Horner s syndrome Pantopaque myelography performed 18 days later yielded clear spinal fluid small bulges in the contrast outline which was convex laterally were present and there was no evidence of the root outline at the level of C 7 C 8 and Th 1 (Fig 5) Roentgen diagnosis Avulsion of the left C 7 C 8 and Th 1

We have also recently demonstrated by pantopaque myelography an extra dural arachnoidal cyst which, at first glance, resembled an avulsion pocket The patient was a 53 year old man with myelopathy of unknown origin He had no signs or symptoms referable to the upper extremities and had never

had any injury to the right shoulder A pocket was visible at the level of the right C 8, but directly cranial to it the defect in the contrast outline at the site of the nerve root was intact (Fig 6)

Discussion and Conclusions

In most of the earlier publications main emphasis has been laid on large contrast filled extradural pockets A few remaining nerve fibres are sometimes found in these at operation and hence there is a possibility, although as a rule very slight, that regression of the paralysis may take place

Most patients however have in addition or even exclusively as in our Cases 5 and 6 less marked but equally pathognomonic changes in the root pockets, the characteristic feature consists in the absence of the central defect in the contrast medium corresponding to the position of origin of the nerve root That an avulsion is also present in these cases may be regarded as certain seeing that 7 out of the 12 cases proved by operation (TARLOV's cases 1 and 2 WHITELEATHER's cases 1 and 2, and BORELLI's three cases) displayed this myelographic appearance TARLOV and WHITELEATHER considered that absence of contrast filling in a large pocket is due to the lesion of the dura mater having healed since they had noted after laminectomy, in addition to a complete avulsion in which not a single nerve fibre remained that the dura lesion was replaced by dense scar tissue Other investigators such as RAYLE held that the atypical myelographic appearances may be explained as avulsion without a dura lesion but no operative confirmation of this seems to have been reported

It is thus obvious that a diagnosis of avulsion can only be made by careful pantopaque myelography with clear demonstration of all the *root pockets* belonging to the brachial plexus Air myelography is capable of *demon*strating large contrast filled pockets but less noticeable changes in the *root* pockets cannot be revealed with this technique

Roentgenographic demonstration of avulsions of the brachial plexus is of great *practical* value as it allows an immediate assessment of the *prognosis* and serves as guidance for correct treatment If the lesions can be established, the *patient will be spared* useless surgical intervention, and no particular spontaneous regeneration can be *expected* Pantopaque myelography is therefore indicated in all cases *in which* the condition is suggested

SUMMARY

The myelographic appearances in 6 cases of avulsion of the brachial plexus are described In addition to the typical extradural *contrast filled* pockets less marked changes around the nerve roots are often discernible the *characteristic* feature being absence of the normal defect in the contrast medium at the point of exit of *the nerve root* These changes are equally pathognomonic as the former signs and can only be demonstrated by pantopaque myelography



Fig 4 Case 5 Small bulges in the contrast outline and no signs of root contours at the right C 8 and Th 1 (Cf normal root contours on left side)

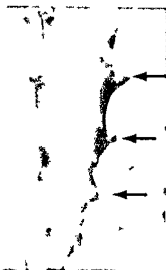


Fig 5 Case 6 Small lateral projections from the contrast outline and no signs of root contours at level of the left C 7 C 8 and Th 1



Fig 6 Extradural arachnoidal cyst in a man aged 53 without clinical signs of avulsion Small contrast filled pocket at the right C 8 but directly above it the defect corresponding to the nerve root is intact

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FROM THE INSTITUTE OF MEDICAL PATHOLOGY AND CLINICAL METHODOLOGY (DIRECTOR PROF CATALDO CASSANO), UNIVERSITY OF ROME ITALY

EXPERIMENTS WITH CHOLECYSTOKININ

by

ALDO TORSOLI MARIA LETIZIA RAMORINO CORRADO COLAGRANDE and GIAMPIERO DEMAIO

Cholecystokinin is a hormone that promotes gallbladder contraction and belongs to the group of 'silent hormones' (so called by JORPES) that control digestion in the upper part of the gastro intestinal apparatus

IVY and OLDBERG first provided evidence that the cholecystokinetic effect of duodenal mucosa extracts is due to a specific hormone of which they obtained the first samples But IVY and OLDBERG s cholecystokinin as well as pancreozymin found many years later by some English workers (DUNCAN et coll) turned out to be of little practical value the preparations moreover caused undesirable side effects In 1954 JORPES and MUTT finally elaborated a method of obtaining highly purified and active preparations suitable for clinical purposes The biologic assay of the hormone is made according to IVY and OLDBERG or by closely related methods The Ivy dog unit is defined as the amount of dried material free of vasodilatatory effects which when dissolved in normal saline solution and injected intravenously within 10 or 15 sec causes within the first three minutes an intra gallbladder pressure rise of 1 cm The cholecystokinetic effect of cholecystokinin is demonstrated in vivo as well as in vitro

The release of the hormone from the duodenal mucosa seems to be connected with the stimulation of a procainsensitive receptor which is connected to the cells producing cholecystokinin by a pathway that can be blocked by hexamethonium (HONG MAGEE and CREWDSON 1956)

Cholecystokinin also causes the relaxation of the sphincter of Oddi an effect

Submitted for publication 20 July 1960

ZUSAMMENFASSUNG

Das myelographische Bild von 6 Fällen von Abrissen des Plexus brachialis wird beschrieben Ausser den typischen kontrastgefüllten Extraduraltaschen sieht man oft kleinere Veränderungen in der Umgebung der Nervenwurzeln wobei das charakteristische Bild der normalen Kontrastmittelaussparung an der Austrittsstelle der Nervenwurzeln fehlt Diese Veränderungen sind ebenso als pathognomonisch anzusehen wie die erstgenannten Symptome und *können nur mittels Pantopaque* Myelographie nachgewiesen werden

RÉSUMÉ

L auteur décrit les signes myélographiques dans 6 cas d arrachement du plexus brachial Outre les poches extra durales typiques remplies par le contraste on observe souvent des modifications moins importantes autour des racines nerveuses caractérisées par l absence de la lacune normale dans le moyen de contraste au point de sortie de la racine Ce dernier signe est aussi pathognomonique que le premier et ne peut être mis en évidence que par myélographie au pantopaque

REFERENCES

Borrelli I J and Maglione A A The importance of myelography in spinal pathology Amer J Roentgenol 76 (1956) 273

Good C A Adson A W and Abbott K H Spinal extradural cysts Amer J Roentgenol 52 (1944) 53

Jaeger R and Whiteley W H Avulsion of the brachial plexus J Amer med Ass 153 (1953) 633

Meredith J M Unusual tumors and tumor like lesions of the spinal canal Virginia med Monthly 67 (1940) 675

Murphey F and Kirklin J W (1949) quoted by Whiteleather

— Hartung W and Kirklin J W Myelographic demonstration of avulsing injury of the brachial plexus Amer J Roentgenol 58 (1947) 102

Passerini A Il quadro mielografico della avulsione delle radici del plesso brachiale Minerva Med 50 (1959) 359

Pendergrass E P Schaeffer J P and Hodes P J The head and neck in roentgen diagnosis Second edition p 1750 Blackwell Scientific Publications Oxford 1956

Rasmussen P Traumatiske plexus brachialislasioner (Danish) Ugeskr Læg 121 (1959) 1215

Rayle A A Gay B B and Meadors J L The myelogram in avulsion of the brachial plexus Radiology 65 (1955) 65

Sassaroli S e Spaccarelli G Il quadro mielografico delle lesioni da strappamento del plesso brachiale Nunt radiol 23 (1957) 388

Tarlov I M and Day R Myelography to help localize traction lesions of the brachial plexus Amer J Surg 88 (1954) 266

White J C and Hanelin J Myelographic sign of brachial plexus avulsion J Bone Jt Surg 36A (1954) 113

Whiteleather J E Roentgen demonstration of cervical nerve root avulsion Radiology 72 (1954) 1017

Wiedenmann O und Decker K Das Myelogramm bei Ausrissen des Armplexus Fortschr Röntgenstr 84 (1956) 345

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IVY and OLDBERG first provided evidence that the cholecystokinetic effect of duodenal mucosa extracts is due to a specific hormone of which they obtained the first samples. But IVY and OLDBERG's cholecystokinin as well as pancreozymin found many years later by some English workers (DUNCAN et coll.) turned out to be of little practical value: the preparations moreover caused undesirable side effects. In 1954 JORPES and MUTT finally elaborated a method of obtaining highly purified and active preparations suitable for clinical purposes. The biologic assay of the hormone is made according to IVY and OLDBERG or by closely related methods. The Ivy dog unit is defined as the amount of dried material free of vasodilatatory effects which when dissolved in normal saline solution and injected intravenously within 10 or 15 sec. causes within the first three minutes an intra-gallbladder pressure rise of 1 cm. The cholecystokinetic effect of cholecystokinin is demonstrated in vivo as well as in vitro.

The release of the hormone from the duodenal mucosa seems to be connected with the stimulation of a procainsensitive receptor which is connected to the cells producing cholecystokinin by a pathway that can be blocked by hexamethonium (HONG, MAGEE and CREWDSON 1956).

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of contraction on this structure, reported by some authors to occur with the crude preparations, is probably due to the presence of a factor different from the hormone which has been proved to produce intestinal contraction (P substance). It was as a matter of fact shown that in vitro purified cholecystokinin preparations have an effect on the gallbladder but not on the intestine of the guineapig, while the P substance is active on the intestine but not on the gallbladder (HULTMAN 1955).

The cholecystokinin preparation of JORPES and MUTT was assayed by IVY and JANECECK (1959) and found to be the most potent preparation ever tested in their laboratory. It contained a small amount of secretin, i. e. from 0.5 to 1 unit of secretin for each unit of cholecystokinin.

Clinical trials with cholecystokinin were first carried out in the Spring of 1955 at Södersjukhuset in Stockholm and a short report on the first results was given by JONSSON in August of the same year. Since then many reports have been published on the subject and the reader is referred to the bibliography accompanying this paper.

Materials and Methods

Radiologic examinations after cholecystokin (Cecekin Vitrum) were carried out in 175 cases.

The total human material consisted of 154 subjects (57 men, 97 women) aged from 12 to 76 years, 44 were normal and 110 presented symptoms referable to the biliary tract. The roentgenologic demonstration of the biliary system was obtained by oral and intravenous cholecystography (121 cases), by barium gastro intestinal examinations (8 subjects with operative choledochoduodenostomy) and by fistulography (25 postoperative examinations).

Routine examinations with serial exposures were used in 56 cases, cinefluorographic methods in 83 cases and cinefluorography combined with simultaneous electromanometric recording of biliary and duodenal intraluminal pressures in 36 cases.

The material was divided into the following groups:

A. One cholecystokinin test (107 cases).
B. Various doses and methods of administration of the hormone (5 cases).
C. Egg yolk meal and cholecystokinin (20 cases).
D. Egg yolk meal and various doses and methods of administration of cholecystokinin (22 cases).

The animal material consisted of 21 dogs. The biliary apparatus was filled by intravenous cholecystography in 9 animals and by operative or postoperative cholangiography in 12 animals.

The examinations were carried out by cinefluorography in 9 dogs and by

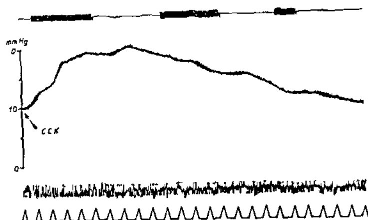


Fig 1 Intra-gallbladder electromanometric pressure curve after cholecystokinin (75 Ivy units/3 min) following cholecystectomy in man From top to bottom synchronization of cinefluorographic exposures intra gallbladder pressure curve respiration diagram and time curve (in minutes)

cinefluorography combined with simultaneous electromanometric recording of intraluminal biliary and duodenal pressure in 12 animals

Cholecystokinin was administered in doses of 1 Ivy unit per kg bodyweight by intravenous injection during 3 min (8 animals), by intravenous perfusion during 30 min (7 animals), and by intravenous injection during 30 sec (6 animals)

The cinefluorographic examinations were carried out with two image amplifiers (Westinghouse and Siemens 5) equipped respectively with a 16 mm Paillard and a 35 mm Arriflex camera and using Kodak Tri X negative film Frames per second 12 16 and 24 Electromanometric recordings were made by two Elema strain gauge manometers connected with a 6 channel recording unit Radiographic serial exposures were obtained at 1, 2 4 8 12 18 24 30 40 60 and 90 min after the beginning of the injection The largest transverse diameter of the gallbladder was measured for the quantitative evaluation of gallbladder emptying (BRODEN) The use of such a comparatively rough method seemed suitable for our purpose in consideration of the large material which was statistically examined

Action of cholecystokinin on the gallbladder

The findings show that in human subjects and in the dog cholecystokinin promotes the contraction of the gallbladder and favours its emptying The effect on the contraction must be distinguished from the degree of emptying the latter though a consequence of the former is not proportional to it but



Fig. 2



Fig. 3 a



Fig. 3 b

Fig. 2. Cholecystography in a normal case 4 min after the injection of cholecystokinin (75 Ivy units/3 min). The cystic and common bile ducts and the choledochoduodenal junction are well shown. The appearance of duodenum is normal.

Fig. 3. Cholecystography in a case with biliary symptoms. a) Before and b) 1 min after beginning of cholecystokinin injection (75 Ivy units/3 min) which caused rapid contraction of the infundibulum: gallbladder became ball shaped.

presents a large variability depending upon the dose and the method of administration of the hormone and upon the individual reactivity of the infundibulum and cystic duct. The effect upon the contraction, demonstrated by a rising electromanometric curve of intracholecystic pressure, tends to be constant. Cholecystokinin produces an active cholecystic contraction in which, after a short period of latency (10 to 30 sec), two successive periods can be distinguished: a period of tension in which the junction of the gallbladder and cystic dust is closed (15 to 60 sec) and a period of expulsion in which the junction of the gallbladder and cystic duct is open (5 to 30 min). This contraction is of the tonic type, no phasic motor events are recorded (Fig. 1).

The effect on the evacuation is marked by a reduction in the gallbladder size and by *filling of the biliary ducts. The emptying is usually* accompanied by an early reduction in the transverse diameter of the infundibulum which in most cases becomes clearly outlined. Throughout the first period (10 min) the reduction in the size of the infundibulum tends to prevail over those of the body and fundus of the gallbladder. Alternative contractions and relaxations are evident and have no counterpart in other tracts. The early and conspicuous filling of the cystic duct and, frequently, of the hepatic ducts is due to this dynamic activity of the infundibulum: even the choledochoduodenal junction is clearly visible (Fig. 2). In some cases, however, the dynamic response may be excessive, in which cases the infundibular cavity becomes smaller and eventually disappears, sometimes, after the normal period of tension, the function



Fig. 4. Cholecystography in a case with biliary symptoms. Effect of amyl nitrite upon hypertonicity of the infundibulum-cystic duct junction induced by overdosage of cholecystokinin (75 Ivy units/30 sec.) (Cineroentgenography.)

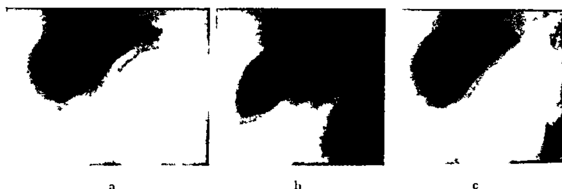


Fig 5 Cholecystography in a normal case a) before fatty meal b) 30 min after fatty meal and c) 12 min from the beginning of the cholecystokinin injection (75 Ivy units/3 min) Marked contraction of infundibulum

of the gallbladder and cystic duct remains closed or recloses after a short period of relaxation, in both cases the gallbladder emptying may be partially or completely blocked (Figs 3 and 4)

These events deserve to be compared with those which follow the administration of the usual fatty meal (Fig 5) Both the period of latency and the periods of tension and expulsion also occur after the egg-yolk meal The various dynamic events, however, progress very slowly and the maximal evacuation is generally reached after at least one hour, these events are intercoordinated, i e the contraction is the result of the balanced participation of the different sectors of the gallbladder (fundus, body and infundibulum) As a rule, the gallbladder is reduced concentrically, the contraction of the infundibulum is evident only at the end of the emptying, the visibility of the ducts is mostly limited to the cystic duct and to part of the common bile duct A fatty meal therefore seems to be a more physiologic means of emptying the gallbladder than cholecystokinin, it makes it possible in fact gradually to produce almost complete evacuation Cholecystokinin, on the contrary, is a prompt and efficient stimulant of gallbladder contraction, especially of the infundibulum (Figs 6 and 7)

It is possible to demonstrate a direct relationship between the dynamic response of the infundibulum and of the junction of the gallbladder and cystic duct and the dose (amount and period of administration) of cholecystokinin

The effects of different doses and different methods of administration were compared in a group of 12 normal subjects and 15 subjects with biliary tract disorders Our findings may be summarized as follows

1 In normal subjects and sometimes also in subjects with biliary disease, cholecystokinin can produce obvious contraction even in doses of a half or two thirds of the standard dose (1 Ivy unit per kg bodyweight injected intra

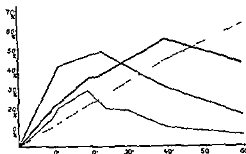


Fig 6 Gallbladder emptying rate in 42 subjects, some healthy and some with biliary disorders after fatty meal (interrupted line) and after cholecystokinin injection 1 Ivy unit/kg bodyweight in 30 sec (thinnest line) 3 min (medium line) and 30 min (thickest line) After the fatty meal the emptying is more gradual and more complete When the hormone is administered by perfusion (30 min) the emptying rate is similar to that produced by the fatty meal The standard cholecystokinin test produces an earlier and shorter gallbladder contraction

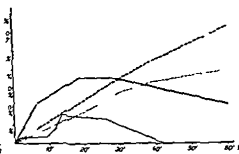


Fig 7 Mean emptying values obtained in 42 subjects 16 healthy and 25 with biliary disorders *after fatty meal and injection of cholecystokinin* The heavy interrupted line indicates fatty meal test in normal subjects and the thinner interrupted line same test in subjects with *functional biliary disorders* The heavy continuous line indicates cholecystokinin injection in normal subjects and the thinner continuous line in subjects with functional biliary disorders

venously in 3 min) or in slowly injected standard doses (0 8 to 2 5 Ivy units per min) In the normal subject a dose of 25 Ivy units injected within 3 min causes *an average 40 % emptying of the gallbladder*

2 The dose that assures in a normal subject the highest degree of gradual evacuation *is 1 Ivy unit per kg (dissolved in about 350 ml of physiologic solu*tion) and administered by intravenous perfusion within a period of 30 min This dose (at the end of the perfusion) causes an evacuation of 50 to 70 % this form of the cholecystokinin test is the one most similar to the egg yolk test from which it however, differs by a clearer outlining of the infundibulum

3 The standard dose administered within the standard period may be used as a test for the functional exploration of the infundibulum In normal subjects this dose produces a definite but not complete contraction of the infundibulum allowing the further partial evacuation of the bile from the fundus and from the body of the gallbladder The gallbladder evacuation, on the whole reaches an average of about 40 % within 20 min

4 Greater doses injected within the standard or shorter periods of time induce abnormal hypertonic *and spastic reactions* of the infundibulum in many normal subjects thereby arresting the evacuation The hypertonic and spastic condition may be prevented or at least partially reduced by the administration of amyl *nitrite*

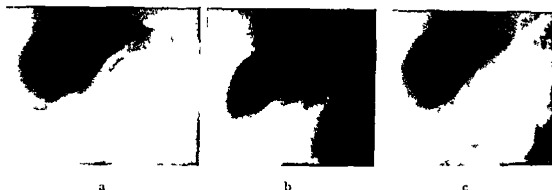


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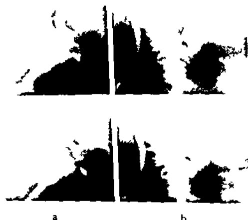
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Fig 9 Cho edoch duodeno tomy follo ng cl lecystectomy Sclero ng odditis Gastro-intestinal c nefluo ograph c e ami nat n a) befo and b) 3 m n aft r th beg nn g of injection of cholecy tokin (75 Ivy un t /3 min) Relaxat on of upper part of Oddi apparatu



F 10 Hyperto city of the sp incter of Odd followin lo y t tomy Intracho doch l probe n s tu a) d r ng t c ally nduc d l yp rpres re (30 cm H O) and b) du g normal perfus on pressure (14 cm H O) after hole y t n n (75 I y units/3 min) Th c nefluo ographic frames rrespond g to exam nation performed on d ffer nt days ug est that cho ecysto in n p oduces b le eflux into the pancreat c d ct

Action of cholecystokinin in the common bile duct and the apparatus of Oddi

Both in human subjects and dogs cholecystokinin seems to cause variations in the tone of the wall of the common bile duct and clearly modifies the normal basal dynamic activity of contraction and relaxation of the lower part of the duct The action of the hormone has also been demonstrated following cholecystectomy, the contraction was sometimes more marked in these cases than in normal cases, a fact which suggests a direct action upon the muscular structure of the duct

The variations in the shape and pressure of the duct (registered by cinefluorography and by electromanometry respectively, and apparently independent of the bile flow through the duct) have been interpreted as variations in tone of the common duct walls The main effect of cholecystokinin on the apparatus of Oddi is relaxation (Fig 8) According to BOYDEN, the apparatus comprises the common channel (extra and intramural), the pancreatic duct and the common channel musculature, in some cases a common tract of the bile and pancreatic ducts exists Even when the intramural part is organically obstructed, the relaxation induced by cholecystokinin is still evident in the extra mural part (Fig 9) Relaxation sometimes involves opening movements of Oddi s muscles these movements become more and more frequent and start 30 sec to 1 min after the beginning of the in

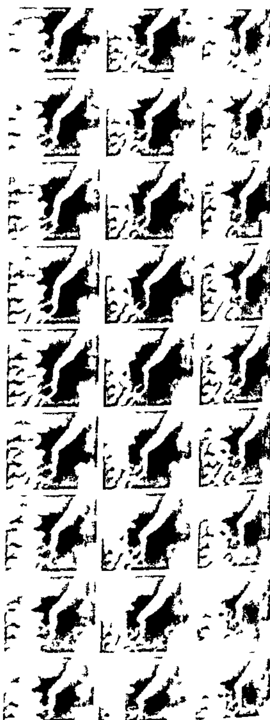
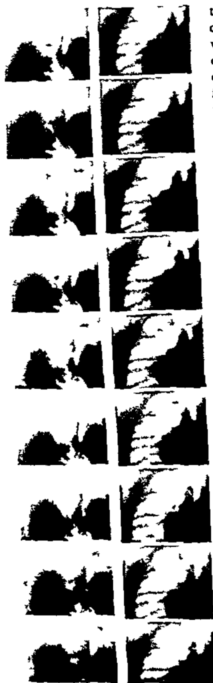


Fig 8 Choledochoduodenostomy following cholecystectomy Gastro intestinal cinefluorographic examination showing effect of relaxation induced by cholecystokinin (75 Ivy units/3 min) on the sphincter of Oddi



the transverse mucosal folds and only occasional peristaltic waves antiperistaltic waves and pendular movements The duodenal content tends to collect in the superior duodenal loop and the superior and inferior functional sphincters of the duodenum sometimes have a hypertonic appearance (Figs 12 and 13)

These morphologic and dynamical aspects are quite different from what is generally seen in gastro-intestinal examinations when the duodenum is filled by barium emulsion through the stomach As shown by the present investigations these aspects are connected not only with the specific hormonal stimulation but also with the mechanical stimulation of the second part of the duodenum produced by its filling through the common bile duct. The tonic relaxation comes after a period of latency which is sometimes associated with a transient activation of motility the same considerations previously made for the activity of the common bile duct hold true for the interpretation of this finding

Experiments carried out in our laboratory (RAMORINO et coll unpublished data) suggest that cholecystokinin also stimulates biligenetic activity The administration of the hormone induces in fact an increase of the bile flow out of a probe inserted in the common duct of cholecystectomized dogs. The increase of flow starts 3 minutes after the beginning of the hormone injection and lasts about 20 minutes The pH and biliary pigments content of the bile increase after cholecystokinin administration

Fig 13 Choledochoduodenostomy following cholecystectomy Gastro-intestinal cinefluorographic examination a before and b 3 min after beginning of the injection of cholecystokinin (3 Ivy units 3 min Characteristic appearance of duodenum.



Fig 11 a Fig 11 b Fig 11 c Fig 12

Fig 11 Cholegraphy in a case with biliary symptoms Hypertonic odditis a) Before b) 2 min and c) 4 min after the beginning of injection of cholecystokinin (75 Ivy units/3 min) Relaxation of terminal part of common bile duct produced by the hormone

Fig 12 Cholecystography in a case with biliary symptoms The exposure was made 5 min after the injection of cholecystokinin (75 Ivy units/3 min) The contrast medium tends to collect in the superior duodenal loop

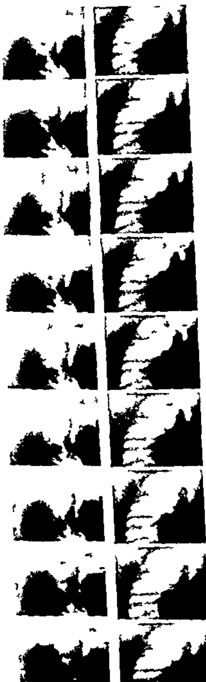
jection Relaxation is occasionally followed by a period (lasting some minutes) in which the common duct is completely patent

The fact that in operative cholangiography, with the perfusion pressure constant, cholecystokinin usually produces a pancreatic reflux suggests a direct effect upon the pancreatic duct (Fig 10) Cholecystokinin may at least temporarily reduce pure Oddi hypertonicity or the functional component of hypertonic odditis (Fig 11) As demonstrated by JACOBSSON and co workers, even spasm of the sphincter induced by morphine is relieved by cholecystokinin, which must therefore be considered as the most powerful relaxing agent of the sphincter of Oddi we have to day

The reasons why before relaxation the terminal part of the common duct remains closed for about 30 to 60 seconds are not yet understood There is some evidence that this is only a period of latency of the hormone action, while other experiments indicate that it is a period of active contraction of the sphincter Present results suggest that an active closure movement may exist when there is a hypertonic condition of the sphincter or when greater or more concentrated amounts of cholecystokinin are used This subject deserves more adequate studies It is connected also with the presence in cholecystokinin preparations of slight traces of substance 'P' and of other agents likely to give rise to the motor tonic activity of the duodenum and sphincter of Oddi

Action of cholecystokinin on the duodenum

Cholecystokinin induces a tonic relaxation of the second part of the duodenum After the injection of the hormone the duodenal loop assumes unusual radiologic appearances characterized by distension, marked prominence of



the transverse mucosal folds and only occasional peristaltic waves, antiperistaltic waves and pendular movements The duodenal content tends to collect in the superior duodenal loop and the superior and inferior functional sphincters of the duodenum sometimes have a hypertonic appearance (Figs 12 and 13)

These morphologic and dynamical aspects are quite different from what is generally seen in gastro intestinal examinations when the duodenum is filled by barium emulsion through the stomach As shown by the present investigations these aspects are connected not only with the specific hormonal stimulation but also with the mechanical stimulation of the second part of the duodenum produced by its filling through the common bile duct The tonic relaxation comes after a period of latency which is sometimes associated with a transient activation of motility the same considerations previously made for the activity of the common bile duct hold true for the interpretation of this finding

Experiments carried out in our laboratory (RAMORINO et coll unpublished data) suggest that cholecystokinin also stimulates biligenetic activity The administration of the hormone induces in fact an increase of the bile flow out of a probe inserted in the common duct of cholecystectomized dogs The increase of flow starts 3 minutes after the beginning of the hormone injection and lasts about 20 minutes The pH and biliary pigments content of the bile increase after cholecystokinin administration

Fig 13 Choledochoduodenostomy following cholecystectomy Gastro-intestinal cinefluorographic examination a) before and b) 5 min after beginning of the injection of cholecystokinin (75 Ivy unit /3 min) Characteristic appearance of duodenum

Conclusions

It has been stated by numerous authors that cholecystokinin reduces the time necessary for cholecystographic examinations, and produces good filling of the excretory ducts and, at least in part, facilitates a subsequent roentgenologic examination of the stomach Our experience, however, suggests that cholecystokinin cannot always take the place of the usual fatty meal It would appear that the indications for the cholecystokinin hormone and the egg yolk meal are different and that in many cases the two tests may be integrated

The administration of cholecystokinin (1 Ivy unit per kg bodyweight intravenously) is indicated in patients unable to take fats or with obstruction symptoms in the esophagus, stomach, or duodenum or in the study of the functional behaviour of the sphincter of Oddi A choledochokinetic test to show whether the choledochoduodenal junction is normal, and to show the functional component of a possible narrowing of the sphincter of Oddi, may be performed with cholecystokinin In all other cases the cholecystokinin test must be carried out only as a supplement to the usual fatty meal test After the latter has been performed, the hormone test seems indicated in the following conditions

1 When the fatty meal test gives normal results, but the existence of a motor dysfunction of the biliary tract is clinically suspected A normal fatty meal test and a limited or interrupted evacuation of the gallbladder or of the common bile duct after cholecystokinin are signs of alterations of the infundibulum cystic duct junction or of the sphincter of Oddi

2 When the response to the fatty meal is poor or negative If the presence of extra biliary factors (such as alterations in the stomach or duodenum) is excluded, a normal response to cholecystokinin is evidence of primary gall bladder hypotonicity, poor or no response to the hormone is, on the contrary, evidence of hypertonic stasis or of hypokinesis due to muscular deficiencies In the first case emptying may be assisted by an inhalation of amyl nitrite

3 When motor dysfunctions of the biliary tract have been found following gastrectomy Cholecystokinin may then be useful in determining if the disorders are caused by alterations in the biliary tract or by an abnormal elaboration of cholecystokinetic agents

Finally, it would appear that cholecystokinin may be of value in the therapeutic field for the continued treatment of patients with primary cholecystic atonia or with biliary stasis of the common duct due to a hypertonic condition of the sphincter of Oddi

Preliminary results seem to support the hypothesis that cholecystokinin exerts an action also on choleresis

Acknowledgement

The authors are grateful to Prof JORPES for his encouragement and advice and to Vitrum AB for the generous supply of the cholecystokinin preparations

SUMMARY

The effects of cholecystokinin on the gallbladder common bile duct and duodenum were investigated in 154 human subjects and 21 dogs by routine roentgenography cinefluorography and electromanometry The results obtained by using different doses and different methods of administration are reported and the cholecystokinin test is compared with the traditional fatty meal test in roentgenologic examinations of the biliary tract

ZUSAMMENFASSUNG

Die Einwirkung von Cholecystochinin auf die Gallenblase die Gallengange und den Zwolffingerdarm ist bei 154 Patienten und 21 Hunden mit Hilfe von rutinmassiger Rontgen untersuchung Kinofilm und Elektromanometrie untersucht worden Die Resultate die man mit Hilfe verschiedener Dosen und verschiedener Administrierungsmethoden erhielt werden berichtet und der Cholecystochinintest wird mit der ublichen Fettmahlzeit bei rontgenologischen Untersuchungen der Gallenwege verglichen

RÉSUMÉ

Les effets de la cholécystokinine sur la vesicule biliaire le cholédoque et le duodénum ont ete études sur 154 sujets humains et sur 21 chiens par la radiographie simple la cineradiographie et l électromanométrie Les auteurs présentent les resultats obtenus avec differentes doses et differentes méthodes d administration et comparent le test à la cholécystokinine au test traditionnel par le repas gras pour l examen radiologique des voies biliaires

BIBLIOGRAPHY

ADLERCREUTZ E JORPES E MUTT V et WEGELIUS C L emploi de la cholécystokinine dans la cholécystographie Arch Mal Appar dig 46 (1957) 414

ALLEGRI A BALDRIGHI V e MONTEMARTINI C Effetti della colecistocinina sulla dinamica delle vie biliari con particolare riguardo al comportamento degli sfinteri colecistico e ledocico Arch Sci med 82 (1957) 656

BARONCHELLI A PIERAGNOLI E e GIRO C La colecistocinina nella pratica del sondaggio duodeno biliare e della colecistografia C Clin med 39 (1958) 1887

BOSSI R La colecistocinina ormone della colecisti nella radiodiagnostica Gazz sanit 30 (1959) 50

BOYDEN E A The anatomy of the choledochoduodenal junction in man Surg Gynec Obst c *104 (1957) 641*

BRODÉN B Experiments with cholecystokinin in cholecystography Acta radiol 49 (1958) 2

CASSANO C TORSOLI A e ALESSANDRINI S Aspetti dinamici di fisiologia e di *fisiopatologia* biliare Nota preliminare Rass Fisiopat clin ter 31 (1959) 609

— — — Aspetti dinamici di fisiologia e fisiopatologia biliare Atti del XIII Congr Soc It Gastroenter Bologna 1959

DUNCAN P R EVANS D G HARPER A A and coll The use of the cholecystokinetic agent in preparations of pancreozymin to study gallbladder function in man J Physiol 121 (1953) 19

EDHOLM P The emptying of the human gallbladder under the stimulus of cholecystokinin Acta radiol 50 (1958) 521
HONG S S, MAGEE D F and CREWDSON I The physiologic regulation of gallbladder evacuation Gastroenterology 30 (1956) 625
HULTMAN F H A method for the standardization of cholecystokinin in vitro Acta physiol scand 33 (1955), 291
IVY, A C Motor disfunction of the biliary tract Amer J Roentgenol 57 (1947), 1
— and JANECECK H M Assay of Jorpes Mutt secretion and cholecystokinin Acta physiol scand 45 (1959) 220
— and OLDBERG, E A hormone mechanism for gallbladder contraction and evacuation Amer J Physiol 86 (1928) 599
— KLOSTER, G, LUETH, H C and DREWYER, G F On preparation of cholecystokinin Amer J Physiol 91 (1928), 336
JACOBSSON, B Personal communication
JORPES E and MUTT V On the action of highly purified preparations of secretin and pancreozymin Ark Kemi 7 (1954) 553
— — Secretin pancreozymin and cholecystokinin Their preparation and properties Gastroenterology 36 (1959) 337
— — TOMENIUS J och BACKLUND V Cholecystokinin vid rontgenundersokning av gallvagarna (Swedish) Svenska Lak Tidn 54 (1957) 2736
— — — and BACKLUND V Cholecystokinin in roentgenologic examination of biliary tract Rontgenblatter 11 (1958) 145
JONSSON S (1959) Private communication
OLIVA L L impiego della colecistocinina in colecistografia Radiologia 15 (1959) 193
PELLEGRINI, G ALLEGRI A BALDRIGHI V e MONTEMARTINI C Valutazione della dinamica biliare con la puntura colecistica transepatica Arch Sci med 82 (1957) 677
POTTS D G Demonstration of the bile ducts with pancreozymin Brit J Radiol 32 (1959) 701
RAMORINO M L COLAGRANDE C MONTI G e SISTI P Effetti della colecistocinina su l apparato biliare extraepatico e sul duodeno Arch Mal Appar dig 27 (1960) 403
STIRIS G Cholecystokinin ved gallevelsundersokelser (Norwegian) T norske Laegeforen 78 (1958) 634
TOMENIUS J och BACKLUND V Cholecystokinin vid rontgenundersokning av gallvagarna (Swedish) Nord Med 61 (1959) 41
YOUNG F T and GREENGARD H Response of the isolate gallbladder to cholecystokinin Amer J Physiol 103 (1933) 275

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF J FRIMANN DAHL) ULLEVAL HOSPITAL, OSLO NORWAY

NORMAL VARIATIONS OF THE LEFT KIDNEY

An anatomical and radiologic study

by

J Frimann Dahl

The kidneys are parenchymatous organs situated in the retroperitoneal space close to the posterior abdominal wall at the level of the second and third lumbar vertebrae PERNKOPF estimates the average size of the kidneys as 12 cm long 6 cm broad and 3 cm thick and states that there is a certain difference in shape and size the left kidney being somewhat larger than the right The weight varies from 150 to 200 g The axis of the kidney is obliquely positioned in both the sagittal and frontal planes and lies parallel to the surface of the psoas muscle Its position varies with the contraction of the psoas and also with the respiratory movements of the diaphragm

The kidneys are described in anatomical textbooks as a pair of almost symmetrical organs It is indicated however that there are some small differences between the right and the left kidney It is well known that the left kidney lies from 1 to 10 cm higher than the right but normally this arrangement may be reversed with the right kidney a little higher than the left The kidney is situated more caudally on the right side than on the left mainly because the liver intervenes and occupies most of the right hypochondrium

The dorsal surface of the kidney is in contact with the posterior abdominal wall lying against the psoas muscle the diaphragm, and the quadratus lumborum muscle On the posterior surface there are some more or less marked

Submitted for publication 3 May 1960

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HONG, S S, MAGEE, D F and CREWDSON I The physiologic regulation of gallbladder evacuation Gastroenterology 30 (1956) 625
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— and JANECECK, H M Assay of Jorpes Mutt secretion and cholecystokinin Acta physiol scand 45 (1959) 220
— and OLDBERG E A hormone mechanism for gallbladder contraction and evacuation Amer J Physiol 86 (1928) 599
— KLOSTER, G LUETH H C and DREWYER, G L On preparation of cholecystokinin Amer J Physiol 91 (1928), 336
JACOBSSON B Personal communication
JORPES E and MUTT V On the action of highly purified preparations of secretin and pancreozymin Ark Kemi 7 (1954) 553
— — Secretin pancreozymin and cholecystokinin Their preparation and properties Gastroenterology 36 (1959) 337
— — TOMENIUS J och BACKLUND V Cholecystokinin vid rontgenundersökning av gallvagarna (Swedish) Svenska Lak Tidn 54 (1957) 2736
— — — and BACKLUND V Cholecystokinin in roentgenologic examination of biliary tract Rontgenblatter 11 (1958) 145
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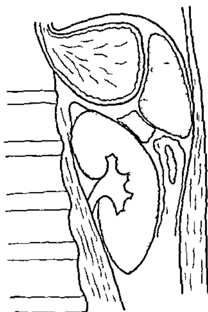


Fig 2 Schematic drawing showing pancreas intervening between the kidney and spleen (modified after PERNKOPF)

The fact that a floating kidney is more rarely encountered on the left than on the right side is probably associated with this feature The fixation of the left kidney may also be explained by the fact that it is anchored by its main artery which is shorter than the right (the vein is longer on the left side)

LOFGREN in his anatomical studies showed that the kidney could be divided in three lobes corresponding to three segments, there were three calyces (and pyramids) in the upper lobe two in the middle lobe (double pair, ventral and dorsal) and two in the lower lobe BOIJSEN used a similar classification in his anatomical studies of the vascular pattern The same division has been adopted by SEMB and FRIMANN DAHL in various works on diseases of the kidneys

Roentgen appearances

MOELL, in his roentgen study on the size of the kidneys states that the kidneys are smaller in women than in men and that in both sexes the left is somewhat larger than the right In men he found the average dimensions to be 12 7 cm × 6 3 cm for the right kidney and 13 2 cm × 6 4 cm for the left the total area being 129 6 cm² and the area per sq meter of the body surface 70 1 cm² The corresponding figures for women are 12 4 cm × 5 9 cm, 12 8 cm × 6 1 cm and 119 3 cm² and 72 2 cm² respectively

In conventional pyelography only the pelvis and the calyces are properly demonstrated The parenchyma and the outer contour are better shown by urography and particularly if the ureter is blocked as for instance in cases of ureteric stones Due to accumulation of the contrast medium a so called nephrographic effect is obtained and this provides an opportunity to determine the outer contour and shape of the kidney By aortography a similar loading of the parenchyma may be observed and the spleen is also rendered opaque (Fig 3) Selective renal angiography produces more marked density (Fig 4a) and the size and shape of the kidneys may be studied accurately oblique views may prove of value (Fig 4b) This procedure has in turn stimulated the study of the vascular anatomy of the kidneys including the cortical pattern

The present study is based on a series of 250 selective renal angiographies and an estimated 5 950 urographies carried out over the last three years

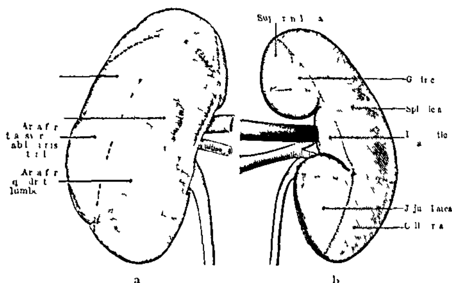


Fig. 1. a) Dorsal aspect of left kidney. Slight impressions caused by muscles and tendons upon which the kidney rests. r — impression of the last rib. b) Ventral surface of the left kidney showing different areas of neighbouring organs.

depressions caused by the muscles and tendons upon which the kidneys rest. When the kidney is fixed and hardened before removal, smooth elevations and ridges are occasionally observed, but usually they are not sharply defined. According to CUNNINGHAM, there is in addition to these facets on the posterior aspect often a small groove for the last rib, one for the lumbo-costal arch, and two or three minor depressions for the upper transverse processes of the lumbar vertebrae (Fig. 1 a).

The ventral syntopy (Fig. 1b) is more complicated. On the right side the liver overlies the kidney anteriorly and laterally and only the posterior part is in contact with the kidney, forming the area hepatica. There is sometimes a duodenal area as well.

On the anterior surface of the left kidney three more or less defined flattened impressions are found. One of these is the splenic impression. The spleen is usually in contact with the kidney on its lateral and anterior border, but this varies largely according to the size of the spleen. Occasionally the tail of the pancreas may intervene, partly separating these organs (Fig. 2). The pancreas sometimes touches the upper pole of the kidney so that this area is slightly flattened. The stomach is only partly in contact with the kidney since the pancreas and part of the suprarenal gland intervene. Extending downwards to the lower end of the kidney is a facet for the jejunum and the colon. CUNNINGHAM further states that it is common to find the left kidney thicker and less flattened anteroposteriorly than the right, with the impressions upon its surface better marked. In this connection the fixation of the kidneys may also be mentioned.

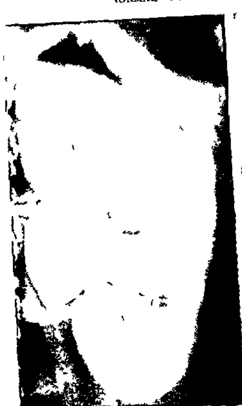


Fig 5 Marked bump in a relatively large kidney and small spleen



Fig 6 Bulging of lateral contour in a relatively small kidney and a large spleen

The study indicates that in about 10 per cent of cases the left kidney has a more or less marked bulging which may vary in position along the lateral border It is usually most conspicuous in the middle segment and when marked gives the kidney an almost triangular form (Fig 5)

The bulge is most evident in adults and in the normal sized kidney but even in small children a tendency to a similar deformity may be observed In practically all cases where this deformity was present the spleen was lying closely adjacent with its renal facies parallel to the lateral border of the kidney The lower pole of the spleen was placed just above and lateral to the elevation or bump Fig 6) The obvious explanation therefore seems to be that the kidney in these cases has to carry the spleen on its back and consequently an indentation is formed so marked that a tumor like elevation occurs If unrecognized this deformity may easily be mistaken for a cyst or even a malignant tumor In cases of unexplained hematuria and a coincidental bulging of the left

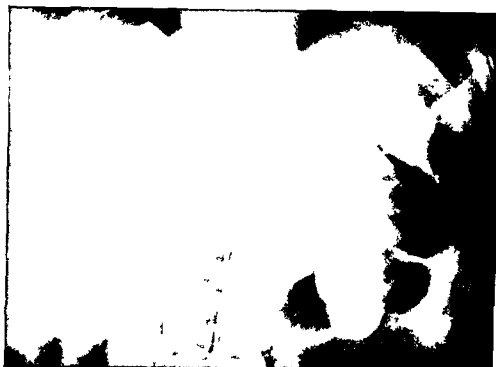
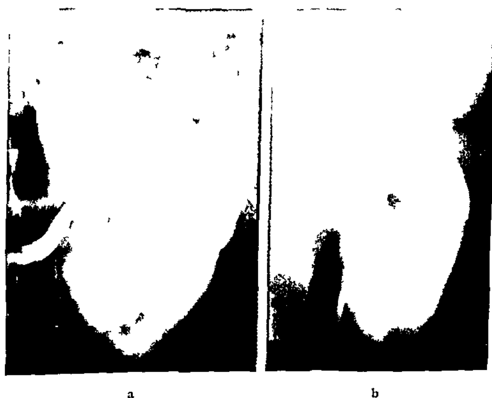


Fig 3 Urography in the course of aortography Contrast medium in the kidneys and spleen



a b

Fig 4 a) Selective renal angiography showing bulging of the lateral contour b) Lateral view of kidney

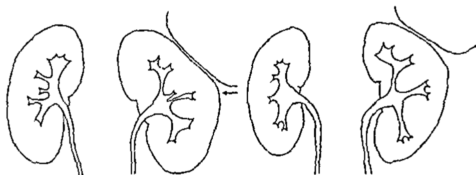


Fig 8 Diagrammatic representations of typ cal normal variations of the calyces of the middle lobe of the left kidney

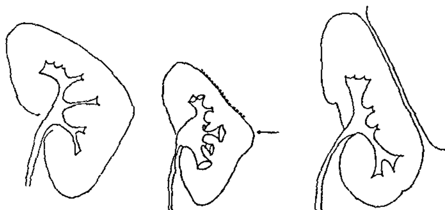


Fig 9 Drawings show ng influ nce of the spleen upon the renal pel is

Fig 10 Normal variation of the upper middle and lower lobe calyces

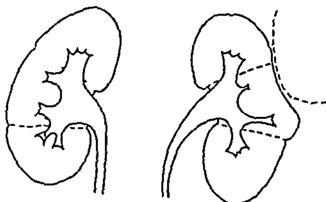


Fig 11 Schematic drawing show g bulg ng of lateral contour of a lobulated left kidney

kidney, for example, misinterpretation may easily be made (Fig 7)

Another important feature is that the kidney pelvis also shows a 'normal' anatomical variation which corresponds to the deformity of the lateral contour The pelvis may be only slightly influenced but the calyces are often markedly changed Different patterns observed in this material are presented in Fig 8 As shown by the schematic drawings, it is mostly the calyces in the middle segment which are influenced When the spleen is lying along the border, one or two calyces of the middle lobe are shortened and the kidney elongated The lower middle calyx, which corresponds to the 'bulging', however, is elongated and larger than normal (Fig 9) Occasionally the calyces of the upper and lower segments are also affected, being either compressed or elongated (Fig 10) If the left kidney presents marked lobulation the bulging may be particularly accentuated (Fig 11)



Fig 7 Bulging of the left kidney Differentiation from a cyst or tumor is important.

Amongst other possible causes of this deformity, the position of the pancreas must be taken into consideration As illustrated earlier in the drawing in Fig 2, the tail of the pancreas may intervene between the spleen and the left kidney However, if the 'bump could be explained as a pancreatic impression, one would expect an enlarged space between the spleen and the kidney in these cases This has not been observed, on the contrary the organs tend to lie closely adjacent A third possibility is an impression caused by the 12th rib As shown in Fig 1a, a depression corresponding to the 12th rib is present but visible only on the posterior surface of the kidney and can therefore hardly interfere with the lateral contour The roentgen findings have been scrutinized with this point in view and in many cases the 12th rib has been found to lie a considerable distance from the bulging or has been poorly developed It therefore seems reasonable that this explanation may also be ruled out The fact that the calyces are influenced by the deformity seems to prove that it must have developed early, probably at a fetal stage A concise morphologic explanation cannot be offered in this study

Whether the deformity of the left kidney is caused only by 'normal spleens is a question difficult to answer and so is the question of the nature of the relationship in very small or enlarged spleens Further experience is required However, there is certainly a wide range of variation, for instance in cases in

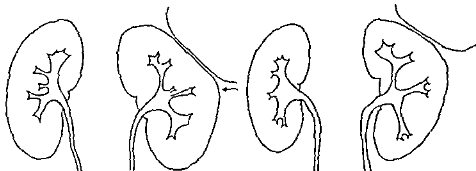


Fig 8 Diagrammatic representations of typical normal variations of the calyces of the middle lobe of the left kidney

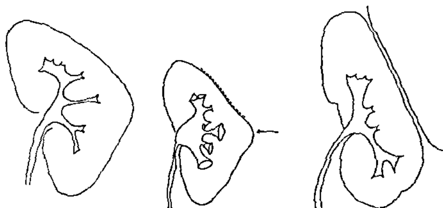


Fig 9 Drawings showing influence of the spleen upon the renal pelvis

Fig 10 Normal variation of the upper middle and lower lobe calyces

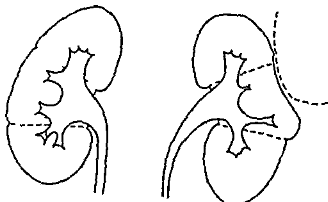


Fig 11 Schematic drawing showing bulging of lateral contour of a lobulated left kidney



Fig 12 Enlarged upper pole of left kidney in combination with a small spleen

which the spleen is nearly invisible and the left kidney lies close to the cupola of the diaphragm The upper pole of the kidney may be correspondingly enlarged, having obviously encroached upon the space of the spleen In such cases the left kidney is much larger than the right (Fig 12)

In other cases an enlarged spleen may have displaced the left kidney downwards and the deformity of the kidney which existed before the enlargement of the spleen is unchanged Under these circumstances the left kidney is apt to be smaller than the right

The fact that the spleen increases in size following a large intake of water has also been considered It could have been that the deformity of the kidney was influenced secondarily by excessive fluid We have investigated this possibility in some cases but so far no convincing results have been obtained

Changes in the vascular pattern are, as a rule, not very conspicuous in relatively small bulgings, in other cases the vessels may be somewhat elongated or stretched in the area of the deformity (cf Fig 8) When there is a marked depression mainly of the upper lobe the vessels are shortened and tortuous (Fig 13)

Finally, one may ask if a similar bulging occurs on the right side It would not be surprising if the large overlying liver caused a deformity of the right kidney but evidently the liver lies more anteriorly than the spleen and does not

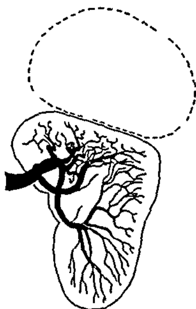


Fig 13 Diagrammatic representation of the vascular pattern in a kidney with a marked splenic impression



Fig 14 Bulging of lateral contour of right kidney (one of the few observed in the period of the investigation)

influence the right kidney in the same way In this series only one case of marked bulging of the right kidney was observed which to some extent was comparable to the findings on the left side (Fig 14)

As far as the author is aware these observations on the appearances of the lateral contour of the left kidney and in many cases corresponding deformity of the pelvis and calyces and changes in the vascular anatomy have not previously been described

SUMMARY

A peculiar deformity of the left kidney occurring in about 10 per cent of all cases is described This consists in a bulging of the lateral contour of the kidney with corresponding changes in the calyces in some cases the vascular pattern is also influenced The deformity is probably secondary to an impression made by an overriding spleen

ZUSAMMENFASSUNG

Eine eigentümliche Deformierung der linken Niere wie man sie in ca 10 % aller Fälle sieht, wird beschrieben Es handelt sich um eine Ausbuchtung der lateralen Nierenkontur mit entsprechenden Kalyxveränderungen. In einigen Fällen besteht auch eine Beeinflussung des Gefässnetzes. Die Deformierung ist wahrscheinlich Folgeerscheinung einer Impression die durch eine überreitende Milz verursacht wird

RÉSUMÉ

L auteur décrit une déformation particulière du rein gauche qui existe dans environ 10 pour cent des cas Elle consiste en une saillie du contour latéral du rein, avec des modifications correspondantes des calices dans certains cas, la disposition des vaisseaux est, elle aussi modifiée Cette déformation est probablement secondaire à une empreinte splénique

REFERENCES

BOIJSEN, E Angiographic studies of the anatomy of single and multiple renal arteries Acta radiol (1955) Suppl No 183

CUNNINGHAM, D J Textbook of anatomy Henry Frowde and Hodder & Stoughton Edinburgh Glasgow and London 1917

FRIMANN DAHL J Radiological investigations of urogenital tuberculosis Urol int separatum 1 (1955), 396

LOFGREN, F Das topographische System der malpighischen Pyramiden der Menschenniere Gleerups Lund 1949

MOËLL, H Size of normal kidneys Acta radiol 46 (1956), 640

ÖDMAN P Percutaneous selective angiography of the main branches of the aorta Acta radiol 45 (1956) 1

PERNKOPF L Topographische Anatomie Urban & Schwarzenberg Berlin und Wien 1943

SCHRODER L Kliniske studier over nyrefunktionen hos nephrectomerede (Danish) Diss København 1944

SEMB C The selective principle in the treatment of urogenital tuberculosis Partial resection of the kidney and of the ureter Urol int separatum 1 (1955) 359

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR PROF SOLVE WELIN)
MALMO ALLMANNA SJUKHUS MALMO SWEDEN

INFLUENCE OF SOME CHOLECYSTOGRAPHIC MEDIA ON THE SIZE OF THE GALLBLADDER

by

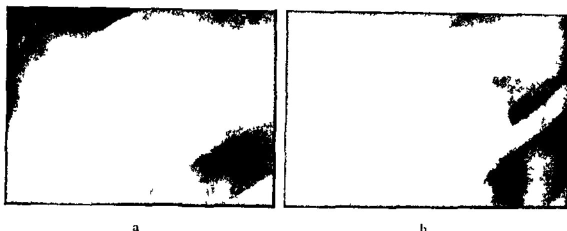
LARS ANDREN and GEORG THEANDER

Much work in recent years has been aimed at comparing the diagnostic value of various cholecystographic media but no attention seems to have been paid to the influence of such media on the size of the gallbladder We have found that cholecystographic media differ characteristically in this respect and some observations are briefly reported and discussed below

Iodoalphionic acid (Bilitrast) iopanoic acid (Telepaque) and its sodium salt (Biliodon Natrium below abbreviated to Bi Na) Biligrafin and Biligrafin forte have been used at the same time or alternately for routine cholecystography in our department for the last 8 years

The number of examinations performed with these media exceeds 20 000 We received the general impression that the gallbladders demonstrated with Bilitrast Biligrafin or Biligrafin forte were on the average larger than those examined with any of the other media mentioned To check this impression we compared films of a total of 30 cases examined on different occasions with different contrast media This group included no cholecystograms showing so-called eccentric contractions of the gallbladder since this phenomenon is accompanied by a diminution in the size of the gallbladder (ANDREN & THEANDER 1958) The interval between the examinations thus compared varied from a few days to several months

Submitted for publication 22 September 1960



a b

Fig 1 Cholecystography with a) Biliodon Natrium and b) Bilitras

Results

The differences in size of the gallbladder were often striking (Fig 1), and the apparent effect of various contrast media seemed to support the original observation (see Table) On the other hand, comparison of the sizes of individual gallbladders on repeated examinations with one and the same contrast medium showed but slight differences and then only occasionally (Table) Furthermore, 27 cases in which the gallbladder had been demonstrated with Bi Na were re examined after a week with Bilitrast No 'eccentric contractions' were present on either occasion In 24 of the 27 cases, the gallbladder was definitely larger when demonstrated with Bilitrast In the remaining 3 cases, no definite size difference occurred

The combined effect of different contrast media was first studied in a few cases after simultaneous administration of Bilitrast and Bi Na In these the resultant size of the gallbladder was found to correspond to that obtained with Bilitrast alone In further experiments Biligrafin forte was administered instead of Bilitrast, since the filling process can be watched roentgenographically with

Table

Comparative size of gallbladder related to contrast medium used on repeated cholecystographies
+ larger than −

Case No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Biligrafin (or Biligrafin forte)	+	+	=	=	=	=		+	+	+	+																			
Bilitrast	−	−	=	=	=	=						+	+	+	+	+	+	+	+	+		−		±						
Bi Na (or Telepaque)								−	−	−	−	−	−	−	−	−	−	−	−	−						−	−			±

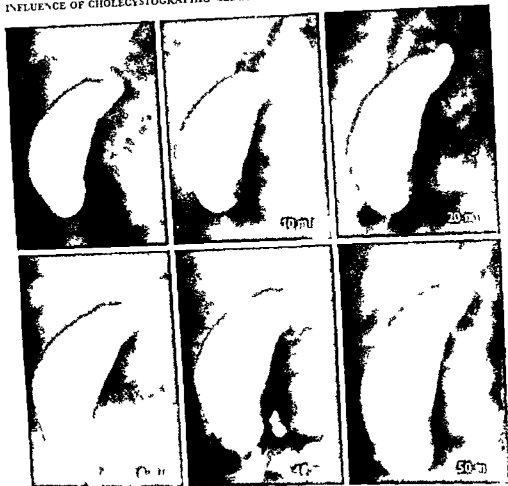


Fig 2 Size of gallbladder on cholecystography with Biliodon Natrium (top extreme left) and the gradual increase at respectively 10 20 30 40 and 50 min after additional administration of Biligrafin forte

the Biligrafin media When Biligrafin alone is used and the gallbladder initially contracted — such as after a fatty meal — filling is sometimes obtained of the gallbladder in the more or less contracted state after which it dilates in association with further inflow of contrast medium (THEANDER 19o6) Eight patients whose gallbladders were demonstrated with Bi Na received 20 ml Biligrafin forte and films were subsequently taken at 10 minute intervals In 7 of them the size of the gallbladder was then seen to increase gradually from that obtained with Bi Na alone (Fig 2)

Discussion

The observations made in the present study show that the size of the cholecystographically demonstrated gallbladder varies largely with the contrast medium used. It is not known whether any contrast medium is inert in this respect but some media apparently differ widely. This should be borne in mind when roentgenographically assessing the normal range of variation of the size of the gallbladder.

The combined effect of various contrast media, differing in their influence on the size of the gallbladder, was apparently the same as when only the medium producing the larger size had been given. This seems to indicate that the effect under discussion is in reality a relaxation. Work in progress on 'eccentric contractions' also suggests the existence of some functional mechanism causing active relaxation of the gallbladder. Nevertheless, the mode of action by which different contrast media produce a different size of the gallbladder is far from properly understood. The physiologic regulation of the size of the gallbladder apparently includes the state of muscular contraction, the supply of fluid via the cystic duct, and the absorptive and secretory functions of the gallbladder mucosa, but current physiologic concepts are unable to explain how these factors co-operate to maintain a suitable gallbladder size. A new approach to this problem might be expected from further roentgenographic and pharmacologic studies of the action of cholecystographic media.

SUMMARY

The gallbladder was observed to be larger when demonstrated with Bilitrast, Biligrafin or Biligrafin forte than with iopanoic acid or its sodium salt. When various media that differed in this respect were given in combination, the larger gallbladder size was obtained.

ZUSAMMENFASSUNG

Es wurde beobachtet, dass die Gallenblase grosser war, wenn sie mit Bilitrast, Biligrafin oder Biligrafin forte dargestellt wurde als mit Iopansaure oder dessen Natriumsalz. Bei kombinierter Anwendung der verschiedenen, unterschiedlich wirkenden Substanzen erhielt man eine grossere Gallenblase.

RÉSUMÉ

Les auteurs ont constaté que la vésicule biliaire est plus volumineuse quand elle est opacifiée par le Bilitrast, le Biligrafin ou le Biligrafin Forte que par l'acide iopanoique ou son sel sodique. Quand on administre en association ces moyens de contraste dont l'effet sur le volume vésiculaire est différent, la vesicule a son plus grand volume.

REFERENCES

ANDREN, L. and THEANDER, G.: Eccentric contractions of the gallbladder in cholecystography. Acta radiol. 49 (1958), 464.

THEANDER, G.: Filling of the gallbladder in cholegraphy. Acta radiol. interamer. 6 (1956), 45.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR PROF SOLVE WELIN) OF THE UNIVERSITY OF LUND MALMÖ ALLMÄNNA SJUKHUS, MALMÖ SWEDEN

UPPER TALAR ENARTHROSIS

by

FOLKE BRAHME

Upper talar enarthrosis seems to be an appropriate name for a condition in which the head of the talus is semiglobular and lies in a socket formed by the lower end of the tibia and the fibula, or the tibia alone The literature contains only 5 cases of this anomaly (LAMB 1958) One further case has been followed since early childhood in our department and will now be reported in some detail

Case report

A man aged 29 with congenital shortening of the right leg combined with genu valgum for which surgical correction (osteotomies on the right femur and tibia) had been attempted twice in early childhood with limited success Roentgen examination when the patient was 3 days old (Fig 1) showed a broad bowed tibia a short fibula and apparently normal arrangement of the tarsal epiphyses A further examination when the patient was 3 years old disclosed a plump talar epiphysis but no signs of a separate navicular epiphysis

He has been complaining of pain in the lower legs and feet and was recently referred for roentgen examination Films obtained of the right and left ankles revealed that the normal ginglymoid joint had been replaced by upper talar enarthrosis The articular surface of the head of the talus was semiglobular and lay in a socket formed on the right side by the tibia and fibula and on the left by the tibia The right tibia was slightly bowed There was no shortening of the fibula but the head of the bone was deformed Bony ankylosis was present between the talus and navicular as well as between the bases of the fourth and fifth metatarsal bones The arches of the right foot were flattened out the axes of the talus and calcaneum lying almost parallel The phalanges of the third toe were short and deformed and hallux valgus was present There was no abnormality of the upper extremities

Submitted for publication 27 September 1960



Fig 1 Right leg and foot a) 3 days old b) 3 years old

The bilateral upper talar enarthrosis was the most uncommon anomaly in this case In two of LAMB's cases the anomaly was bilateral, and in 4 it was combined with tarsal ankylosis, shortening of the lower limb was present in all the cases

Most of the other anomalies observed in our case are fairly common Talo navicular fusion, however, is one of the less usual varieties of fusion in the tarsus (O'RAHILLY 1953) The first definite case of bilateral talo navicular fusion was reported by ANDERSON in 1894 and a second case was not described until 1943 (O'DONOGHUE) Several other cases have, however, been published since then (BOYD 1944, WEITZNER 1946, CHAMBERS 1950, and others) It is widely accepted on the basis of embryologic studies that fusion in the carpus and tarsus is due to defective separation of the condensation centres in the mesenchyma Though a fusion of tarsal bones almost always accompanies upper talar enarthrosis, there appears to be no causal relationship between the two conditions, as such fusion most frequently occurs in the absence of talar enarthrosis One of LAMB's cases had no fusion of tarsal bones A functional relationship between the two conditions does however exist Any bony union between elements of the proximal tarsal bones will impair inversion and eversion of the foot The talus, calcaneum and navicular bones form a functional unit which permits about 20 degrees of eversion and inversion of the foot Owing to the arrangement of the muscles, movements



Fig 2 Right ankle a p Enarthrosis   Fig 3 Right foot Fusions of tarsal and metatarsal bones

in the joints are always combined and any tarsal fusion will severely impair the mobility of the foot the limitation may be compensated in the presence of upper talar enarthrosis but only at the expense of the stability of the ankle

The structure of the foot bones of vertebrates varies widely with numerous variants of the primate primitive plane tibial, intermediate and phalangeal The number of tarsals and phalanges also varies Reptiles including the



Fig 4 Right ankle and foot lateral

archisaurus have only two tarsal bones, the calcaneum and the talus. A similar arrangement exists in mammals, the talus then always forming a hinge joint, a joint of the ball and socket type is never encountered. Enarthrosis cannot therefore be regarded as a sign of regression towards an earlier type of ankle joint.

Acknowledgement

The author wishes to express his thanks to Y. Lowegren and T. Askaner for the zoologic data.

SUMMARY

A case of bilateral upper talar enarthrosis, a rare anomaly of the ankle joint is reported.

ZUSAMMENFASSUNG

Es wird uber einen Fall von bilateral oberen Talus Enarthrosis eine seltene Anomalie des Fussgelenkes, berichtet.

RÉSUMÉ

Présentation d un cas d énarthrose astragalienne supérieure bilatérale anomalie rare de l articulation de la cheville.

REFERENCES

ANDERSON R J The presence of an astralago scaphoid bone in man J Anat 14 (1943) 452
BOYD H B Congenital talonavicular synostosis J Bone Jt Surg 26 (1944) 682
CHAMBERS C Congenital anomalies of the tarsal navicular with particular reference to calcaneo navicular coalition Brit J Radiol 23 (1950) 580
LAMB D The ball and socket ankle joint a congenital abnormality J Bone Jt Surg 40 B (1958) 240
MESTERN J Erbliche Synostosen der Hand und Fusswurzelknochen Erbliches Os tibiale externum Rontgenpraxis 6 (1934) 594
O DONOGHUE D H and SELL L S Congenital talonavicular synostosis case report of a rare anomaly J Bone Jt Surg 25 (1943) 925
O RAHILLY R Survey of carpal and tarsal anomalies J Bone Jt Surg 35 A (1953) 626
TRAITE DE ZOOLOGIQUE (Librairie de l Académie de Médicine) Paris 1958
WEITZNER I Congenital talonavicular synostosis associated with hereditary ankylosing arthropathies Amer J Roentgenol 56 (1946) 185

FROM THE FORMER CHIEF (W HONDIUS BOLDINGH) OF THE X RAY DEVELOPMENT LABORATORY OF N V PHILIPS GLOEILAMPEN FABRIEKEN, EINDHOVEN, HOLLAND

QUALITY AND CHOICE OF POTTER BUCKY GRIDS
PARTS IV AND V

by

W HONDIUS BOLDINGH

IV Focus-grid distance limits

The preceding parts of this series of articles were published in 1959 (BONENKAMP & HONDIUS BOLDINGH) under the same main title Excepting the main title the terminology and symbols in the present paper are those which will be recommended by ICRU IV 4 of which the writer is a member

It is important that the user of a grid of given ratio and focal distance should know the extreme focus grid distances between which it may be employed with reasonable results The author in 1958 gave a graphical method for determining the loss V of primary radiation at a distance c from the centre line of the grid when the focus grid distance f the lateral decentring of the focus, the focal distance f and the ratio R are known The task of the radiologist would be facilitated if he were provided with some indication as to these limits based on the ratio and focal distance of the grid

The most complete information (although too complicated) on each grid would be afforded by an accompanying diagram with two graphs plotting the values of $f < f$ and of $f_2 > f$ as functions of the loss V of primary radiation per cm distance from the centre line The provision of more restricted information would appear to be a better solution and the following definition is therefore presented for linear grids

Submitted for publication 29 April 1960

The extreme focus grid distances (focus grid distance limits) are so determined that a loss of 50 % of primary radiation is sustained at a distance of 15 cm from the centre line of the grid, i.e. at the edges of a film 30 cm in width, when a simultaneous horizontal decentring of 1 cm is taken into account.

Before we adopt this definition we should determine whether at these focus grid distance limits reasonable results will be obtained. The contrast loss which is caused at the film edge by this 50% loss of primary radiation may be calculated by means of the formula of MORGAN. (See also the more comprehensible derivation of this formula with explanation of the symbols Diagram 5, p. 233.)

We call the intensity of the primary radiation on the film I'_p (the prime indicating that the beam has passed the grid) and the scattered radiation I', both with the focus centred. In the case of decentring the focus up to one of the 50 % limits, I'_p and I'_s remain unchanged in the centre line of the image, and at the edges I' remains practically the same, i.e. $I''_s = I'$, (the double prime indicating a position at the edge of the film) whilst I'_p is halved: $I''_p = \frac{1}{2} I'_p$.

According to MORGAN, in the first case

$C = C_p \dfrac{1}{1 + \dfrac{I'}{I'_p}}$ and in the second case $C'' = C_p \dfrac{1}{1 + \dfrac{I''}{I''_p}} = C_p \dfrac{1}{1 + \dfrac{2I'_s}{I'_p}}$

where C_p is the primary contrast when $I' = 0$.

Thus the contrast C'' at the edges is reduced as follows:

$$\frac{C''}{C} = \frac{1 + \dfrac{I'}{I'_p}}{1 + \dfrac{2I'}{I'_p}}, \text{ where } \frac{I'}{I'_p} \text{ relates to the centred focus position.}$$

The value of C''/C is given in Table 1 for various values of I'/I'_p; the relative values of the remaining total radiation I''_t/I'_t at the edges are also shown.

According to this, the contrast at the film edges remains unchanged when the grid absorbs practically all the scattered radiation ($I' = 0$). However this conclusion holds good only when both I'_p and $I''_p = \frac{1}{2} I'_p$ are in the linear part of the density curve of the film. In all cases where the scattered radiation is not completely absorbed ($I' \neq 0$) the contrast at the film edges is reduced due to focussing deviations. If we assume that in general the radiation behind the grid centre will not contain more than 50 % scattered radiation, so that $\dfrac{I'}{I'_p}$ is not larger than 0.5, the contrast loss $1 - \dfrac{C''}{C}$ will not be more than 25 %. For

Table 1

Values of C'/C and the relative total remaining radiation I'/I$_t$ given for various values of I'/I$_p$

I'/I_p	0	0.1	0.2	0.5	1.0	2.0	5.0	∞
C'/C	100	92	86	75	67	60	55	50
I'/I_t	50	55	58	67	75	83	91	100

distances from the film centre less than 15 cm the loss of primary radiation is proportionally less and the contrast loss is *more than proportionally reduced* and wider focus grid distance limits can be applied

All this leads to the conclusion that the 50 % limits may be an acceptable definition especially as it is not obligatory but gives *distance values only for* guidance as regards choice comparison and use of grids

It should be mentioned that the above considerations are based on ideal grid construction the losses at the edges will be *larger if the strips are not* exactly centred or not completely flat However examinations of commercially available grids by means of a photocell revealed that in the case of focussing deviations the influence of these imperfections *is not important*

The author in 1958 calculated the loss of primary radiation, when no horizontal decentring was present the following losses were found

$$V_1 = R\,c\left(\frac{1}{f_1}-\frac{1}{f_0}\right) \text{ and } V_2 = R\,c\left(\frac{1}{f_0}-\frac{1}{f_2}\right)$$

$$\text{so } f_1 = \frac{f}{1+\frac{f\,V_1}{R\,c}} \text{ and } f_2 = \frac{f_0}{1-\frac{f\,V_2}{R\,c}}$$

where V_1 = loss of primary radiation at the lower limit f_1
V_2 = » » » » » » upper » f_2
R = grid ratio
f_0 = focal distance
c = distance from centre line of grid

When $c = 15$ cm and for both limits $V_1 = V_2 = 0.5$ we can write for these values

$$f_1 = \frac{f}{1+\frac{f_0}{30R}} \text{ and } f_2 = \frac{f}{1-\frac{f_0}{30R}}$$

These limits are narrowed by $\frac{1}{R}$ = about 7 % per cm simultaneous average lateral decentring of the focus For parallel grids ($f_0 = \infty$) these formulae

Table 2

Focus grid distance limits f_1 and f_2 in cm as functions of f_0 and R
These values may also be determined graphically by means of Diagram 2

Focal distance f_0	Ratio R				
	3	6	9	12	15
60 cm	38—170 (40—170)	48— 85 (50— 90)	53— 73 (55— 75)	55— 68 (55— 70)	57— 66 (55— 65)
90 cm	48—∞ (50—200)	64—170 (65—170)	72—127 (70—130)	77—113 (75—110)	80—104 (80—100)
120 cm	55—∞ (55—200)	77—310 (75—200)	89—203 (90—200)	96—170 (100—170)	100—154 (100—150)
150 cm	60—∞ (60—200)	88—850 (90—200)	103—280 (100—200)	112—245 (110—200)	120—212 (120—200)
∞ (parallel)	90—∞ (90—200)	180—∞ (180—200)	unsuitable under 200 cm		

50 % loss of primary radiation at 15 cm from the centre line of the grid and with 1 cm average lateral decentring of the focus

are transformed into $f_1 = 30\,R$ and $f_2 = \infty$ The 50 % limits f_1 and f_2 calculated from these formulae are given in Table 2 for various ratios and focal distances, whereby 1 cm lateral decentring is taken into account Rounded off values are shown between brackets (in multiples of 5 up to 75 cm, multiples of 10 from 80 cm upwards, 200 for values above 200 cm)

Cross grids It is obvious that the 50 % limits of linear grids described above are not suitable for cross grids This is illustrated by Diagram 1, where the loss distribution in a 30 × 40 cm image (12″ × 16″) is shown for both types of grids, each with 50 % loss at 15 cm lateral distance from the centre

In Diagram 1, (a) and (b), lines of equal loss of primary radiation are drawn for V = 30, 40, 50 % etc, based on the fact that for each linear grid at each point of the surface the loss is proportional to the distance c from the centre line For both types of grid the loss at A is 50 %

At point B, however, the loss with the linear grid is zero, whereas with the cross grid it is 20/15 × 50 % = 67 %, i e 2/3

At the corners, C, of the linear grid the loss is equal to that at A, namely 50 %, whereas with the cross grid the situation is more complicated at B,

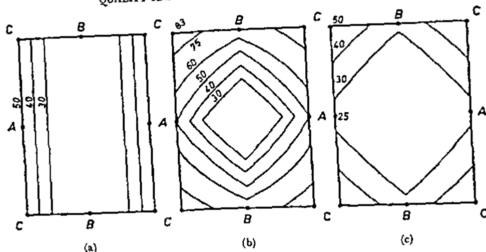


Diagram 1 Distribution of the loss of primary radiation on a 30 × 40 cm film with the tube focus at the focus-grid distance limit

(a) Linear grid with 50	loss in A.	0—30	loss over 60	of total surface
		30—40	» » 20	» » »
		40—50	» » 20	» » »
(b) Cross grid with 50	loss at A. prohibitive			
(c) Cross grid with 25	loss at A	0—30	loss over 55	of total surface
		30—40	» » 36	» » »
		40—50	» » 9	» » »

where the loss is 2/3 there remains one third of the primary intensity, at C this remaining part is halved by the other (crossing) part of the grid so that only one sixth is left the loss at the corners of the cross grid is then 5/6 or 83 % which is prohibitive

If however for the cross grid the loss at A were chosen as 25 % instead of 50 % the remaining part of the primary radiation would be 75 % = 3/4, the loss at B would be 20/15 × 25 % = 1/3 so that two thirds would still remain, and, at C 3/4 × 2/3 = 1/2 would remain i e a loss of only 50 % at the corners

The loss distribution over the whole surface of 30 × 40 cm with a cross grid having a loss of 25 % at A is then slightly better than with a linear grid having a 50 % loss at A as may be seen by comparing (a) and (c) in Diagram 1

If we accept this 25 % definition for cross grids and the 50 % definition for linear grids we can use the same formulae for calculating the focus-grid distance limits of both types provided that for the cross grids we take into account a doubling of the ratio of one of the composing (crossing) grids

The same holds of course for a graphical determination of the focus grid distance limits The graph in Diagram 2 is derived from the more universal one which was published earlier (HONDIUS BOLDINGH 1958 and BONENKAMP & HON

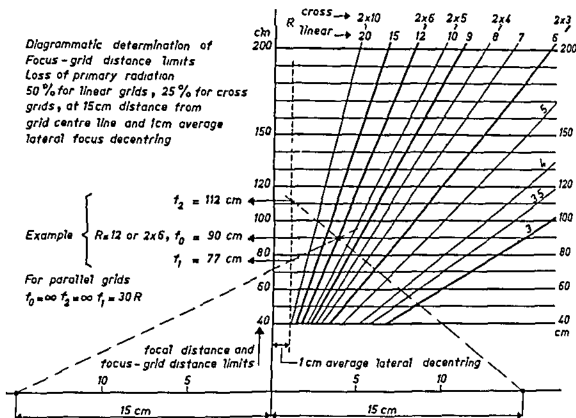


Diagram 2 Determination of focus grid distance limits (50% loss of primary radiation at 15 cm distance from grid centre line and 1 cm average lateral focus decentring) *Instructions* (for the above example) Draw ——— lines through intersection of f_0 line (90 cm) with R line (12) and *read* f_1 (77 cm) and f_2 (112 cm) on intersection of — — lines with vertical ——— line

dius Boldingh 1959, p 249), by an incorporation of the 50 % and 25 % loss definitions for a ready determination of the focus grid distance limits

According to the example given in this graph the same limits (77 and 112 cm) are found for a linear grid with a ratio of $R = 12$, as for a cross grid with $R = 2 \times 6$, both with a focal distance of 90 cm

It may be noted that the definitions for the focus grid distance limits given above have been adopted in the recommendations for grid terminology that are being prepared by the ICRU IV 4 (grids) subcommittee

V The contrast improvement factor

The contrast caused by air and aluminium in water phantoms of various thicknesses and at various tensions have been investigated with and without a grid (Bonenkamp & Hondius Boldingh 1959, p 153) The differences in contrast due to both types of objects have been given and it has been shown that for various grids the influence of these objects reveals itself in a similar way

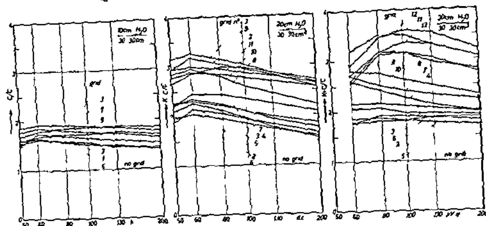


Diagram 3 Contrast improvement factors of 13 grids measured at various voltages with water phantoms of 10, 20 and 30 cm thicknesses

One may now compare the grids by concentrating upon their contrast improving capacity which is independent of the contrast objects. This contrast improving capacity may be evaluated by the contrast improvement factor

$$K = \frac{\text{contrast with grid}}{\text{contrast without grid}} = \frac{C}{C} = T_p \cdot B = T_p/T_t = \frac{\text{transmission of primary radiation}}{\text{transmission of total radiation}}$$

(See Bonenkamp & Hondius Boldingh Part I p 483 and Diagram 5 in this paper.)

This factor is comparable with the definition of the selectivity of the grid (De Waard 1934)

$$\Sigma = T_p/T_s = \frac{\text{transmission of primary radiation}}{\text{transmission of scattered radiation}}$$

But far more than the selectivity the contrast improvement factor is directly and clearly related to what we *want to know* about the grid, namely the contrast improvement as compared to exposures without grid.

The contrast improvement factors of thirteen grids measured at 50, 60, 80, 100, 130 and 200 kV with water phantoms of 10, 20 and 30 cm thicknesses are shown in Diagram 3.

It is hardly possible in practice to discriminate between roentgenograms of the same object made with two grids having contrast improvement factors varying by only a few tenths, e.g. 2.0 and 2.2. Taking this into account the following conclusions may be drawn from the diagrams

Table 3

Grid No		1	2	3	4	5	6	7	8	9	10	11	12	13
Strips cm	cm^{-1}	27	25	24	40	29	24	23	38	24	28	27	22	27
Ratio	—	3.4	2×3.1	7	11	7	6	9	15	2×7	15	15	15	15
Lead	cm^3/cm^2	0.015	0.027	0.030	0.030	0.035	0.038	0.040	0.040	0.060	0.063	0.073	0.079	0.085
content	mm	0.2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.6	0.6	0.7	0.8	0.9
Contrast improvement factor K_{100}		1.95	1.95	2.1	2.1	2.1	1.85	2.35	2.6	2.95	2.8	2.85	2.95	3.0

1 The curves practically do not intersect throughout the whole voltage range This means that there are no grids particularly suitable for low voltages or others for high voltages

2 Within practical limits the sequence of the grids as far as the contrast improvement factor is concerned is the same for various phantom thicknesses This implies that for thinner objects the same grid as for thicker objects may be used, *particularly as according to (1) it is suitable for the whole voltage range*

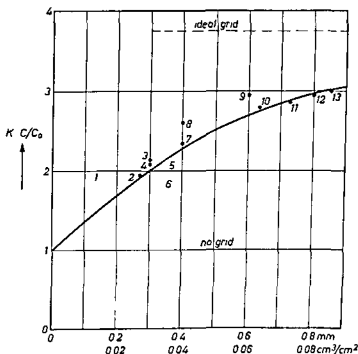


Diagram 4 Contrast improvement factor K_1 (100 kV 20 cm H_2O 30 × 30 cm) as a function of the lead content

Diagram 5 Derivation of contrast formulae

Narrow beam without grid	Wide beam without grid	Wide beam with grid
I_0; H_2O abs coeff μ_1; Contrast object abs coeff μ_2; H_2O; d; I_{p_1} I_{p_2}	I_0; H_2O; I_{p_1} I_S I_{p_2}; $I_{p_1}+I_S=I_t$ $I_{p_2}+I_S$	I_0; H_2O; I_{p_1} I_S I_{p_2}; $I_{p_1}+I_S$ I_p+I_S; $I'_{p_1}+I'_S=I_t$ $I'_{p_2}+I'_S$
I_p = primary radiation	I = scattered radiation	I_t = total radiation
Primary contrast $C_p = \log\frac{I_p}{I_p} = \frac{1}{3}\ln\frac{I_p}{I_p}$ $\frac{I_p}{I_{p_2}} = e^{aC_p}$ where $a = 2.3$	Contrast without grid $C = \log\frac{I_p+I}{I_p+I}$ $\frac{I_p+I}{I_p+I} = e^{aC}$ (1)	Contrast with grid $C = \log\frac{I_p+I}{I_p+I}$ $\frac{I_{p_1}+I}{I_p+I} = e^{aC}$

Further it is obvious that

$$\frac{I_p}{I_p} = e^{d(\;-\;)} = e^{C_p} \qquad = \frac{I_p}{I_p} \quad (2) \qquad = \frac{I_{p_1}}{I_p}$$

From (1) and (2) can be derived by eliminating I_p

$$1 + \frac{I}{I_p} = \frac{1-e^{-C_p}}{1-e^{-aC}}$$

which can be reduced for C_p and C are ⟨⟨1 (small contrasts) to

$$\frac{C}{C_p} = \frac{1}{1+I/I_p} = \frac{I_p}{I} \quad (3)$$

and correspondingly

$$\frac{C}{C_p} = \frac{1}{1+I/I_{p_1}} = \frac{I_p}{I_t} \quad (4)$$

These are the Morgan formulae

The factor $\frac{C_*}{C_p} = \frac{\text{contrast with phantom}}{\text{contrast without phantom}} = \frac{I_p}{I} = \frac{1}{k}$

k could be called the *contrast reduction factor of the phantom*

From (3) and (4) can be derived. $\frac{C}{C} = \frac{\text{contrast with grid}}{\text{contrast without grid}} = \frac{I_p}{I_{p_1}} \Big/ \frac{I_t}{I} = T_p/T_t = K$

where T_p = transmission of primary radiation through the grid
T = » » total » » » »

K may be called the *contrast improvement factor* of the grid

Table 3

Grid No		1	2	3	4	5	6	7	8	9	10	11	12	13
Strips/cm	cm^{-1}	27	25	24	40	29	24	23	38	24	28	27	[illegible]	27
Ratio	—	3.4	2×3.1	7	11	7	6	9	15	2×7	15	15	15	15
Lead content	cm^3/cm^2	0.015	0.027	0.030	0.030	0.035	0.038	0.040	0.040	0.060	0.063	0.073	0.079	0.085
	mm	0.2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.6	0.6	0.7	0.8	0.9
Contrast improvement factor K_{100}		1.95	1.95	2.1	2.1	2.1	1.85	2.35	2.6	2.95	2.8	2.85	2.95	3.0

1. The curves practically do not intersect throughout the whole voltage range. This means that there are no grids particularly suitable for low voltages or others for high voltages.

2. Within practical limits the sequence of the grids as far as the contrast improvement factor is concerned is the same for various phantom thicknesses. This implies that for thinner objects the same grid as for thicker objects may be used, particularly as according to (1) it is suitable for the whole voltage range.

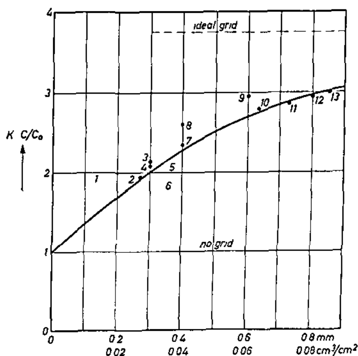


Diagram 4. Contrast improvement factor K (100 kV, 20 cm H_2O, 30 × 30 cm) as a function of the lead content.

RÉSUMÉ

L auteur en partie IV donne la definition des distances limites foyer grille entre lesquelles on peut obtenir de bons resultats Ces limites devraient etre déterminées toujours de la meme façon d apres la distance focale et le rapport de la grille En partie V il propose d adopter un facteur d amelioration du contraste pour evaluer le pouvoir d amelioration du contraste des grilles Ce facteur est plus précis que la teneur en plomb preconisee en partie III car il indique explicitement le rapport entre les contrastes de détail obtenus avec la grille et sans grille

REFERENCES

BONENKAMP J G and HONDIUS BOLDINGH W Quality and choice of Potter Bucky grids I A new method for the unequivocal determination of the quality of a grid Acta radiol 51 (1959) 479 II Application of the criterion of quality to various types of grids III Choice of a Bucky grid Ibid 52 (1959) 149 241

HONDIUS BOLDINGH W Grafische Ermittlung der Verluste an Primarstrahlung infolge unrichtiger Zentrierung und Bewegung von Streustrahlenblenden Fortschr Rontgenstr 89 (1958) 233

MORGAN R H Analysis of the physical factors controlling the diagnostic quality of rontgen images Amer J Roentgenol 55 (1946) 70

DE WAARD R H Die Bedeutung der Selektivitat von Streustrahlenblenden fur die Kontraste im Rontgenbild Fortschr Rontgenstr 50 (1934) 606

3. Within practical limits the shape of all the curves is the same. This means that one point of each curve, chosen at standard conditions, gives a fairly good idea of the relative quality under all working conditions. For these conditions we could choose, for example, a 20 cm standard water phantom and 100 kV d.c.

This characteristic contrast improvement factor, K_{100}, *of the thirteen grids* measured, with their other specific data, i.e. number of strips per centimetre and ratio, are shown in Table 3.

Diagram 4 presents these contrast improvement factors plotted against the lead content. The rough but definite relationship between the contrast improving capacity and the lead content of commercially available grids is evident. Comparing these two characteristic factors and taking into account the above mentioned difficulty of precise discrimination between grids with slightly differing contrast improvement factors *the following statement may be made*: the lead content is a rough but suitable indication of the contrast improving capacity of a grid, being easy to determine and independent of exposure conditions. It is therefore reasonable to refer to 'light', 'medium', and 'heavy' grids when the contrast improving capacity is considered.

The lead content may be evaluated in cm^3/cm^2, e.g. for grid No. 10 it is 0.063 cm^3/cm^2, which may be written 0.63 mm; this means that the lead content is equivalent to a lead sheet of 0.63 mm in thickness. In view of the relationship between the lead content and the contrast improving capacity being only an approximate one, the value may be rounded off to multiples of 0.1 mm and 0.063 cm^3/cm^2 read as 0.6 mm (see Table 3).

The contrast improvement factor is, on the other hand, a more precise qualitative measure but it requires standardized exposure and measuring conditions *for comparable specifications*.

SUMMARY

A specification for grids of the focus grid distance limits between which reasonable results may be obtained is described in Part IV. These limits should always be determined in the same way, according to the focal distance and the ratio. The definition of a 'contrast improvement factor' for the evaluation of the contrast improving capacity of grids is given in Part V. This factor is more accurate than the lead content recommended in Part III because it explicitly indicates the ratio of the detail contrast obtained with and without a grid.

ZUSAMMENFASSUNG

Die Fokus-Raster-*Abstandsgrenzen, zwischen denen man gute Resultate erhalten* kann, werden im Teil IV angegeben. Diese Grenzen sollten stets in gleicher Weise bestimmt werden auf Grund einer Definition des Fokusabstandes und des Schachtverhältnisses. Die *Definition eines Kontrastverbesserungsfaktors* für die Bewertung des Kontrastverbesserungsvermögens von Rastern wird im Teil V gegeben. Dieser Faktor ist genauer als der im Teil III empfohlene Bleigehalt, da er das Verhältnis der Detail-Kontraste angibt, die man mit *und ohne* Raster erhält.

Throughout the work the principle was followed that clinical measurements of dose and dose distribution should be performed as extensively as possible As far as practicable the measurements were carried out as direct dose measurements in patients *Indirect dose measurements* were also used in the form of transit dose measurements The large measured series collected provided good possibilities for assessment of the realizability of the applied clinical measuring program the clinical dose distributions obtained with the different methods and *the value of performing such measurements* in the treatment of intra thoracic as well as of intra pelvic tumours

After a review of the basic procedures and the dose distribution conditions in 200 kV perpendicular axial rotation therapy of intra thoracic lesions a series of *303* patients with carcinoma of the oesophagus is considered 219 of the patients were treated with the method in question The chief reason for this was the desire to present a clinical material to which the principles of precision discussed in the volume were applied This material was investigated in respect to some clinical radiotherapeutic and radiophysical parameters The treatment results are discussed for the total series under investigation for the series of patients treated with rotation therapy and lastly for each of the sub series for the upper middle and lower thirds of the oesophagus

Autore text

DIE PHLEBOGRAPHIE DER UNTEREN EXTREMITAT Von Robert May und Raymund Nissl 137 Seiten und 250 Abbildungen Georg Thieme Stuttgart 1959 Price DM 67 50

Rational management of venous stasis in the legs often requires the performance of phlebography in order to establish a correct diagnosis and obtain clear indications as to adequate therapy in individual cases As varicose veins and post thrombotic conditions constitute the most common of all complaints in civilized countries (one third of all women have varicose veins) their treatment cannot always be carried out at special clinics With a view to arousing a more general interest in and understanding for phlebology the authors of the book under review have endeavoured to present a clear account of the phlebographic features met with in normal and pathologic cases

The first four chapters are devoted to normal anatomy phlebographic technique and problems connected with contrast media It is refreshing to note that the authors do not seem to be ardent advocates of any particular phlebographic method they emphasize the importance as in all other fields of roentgen diagnosis of aiming at exact phlebographic demonstrations of different pathologic changes in the venous system and of modifying the technique to suit the individual cases Unfortunately they made a departure from this rule in the case of retrograde phlebography and left *the treatment of this subject to* J D Martinet of Paris The chapter in which he describes his special method for retrograde phlebography is definitely inferior to the other parts of the book Its illustrations are for the most part incorrectly interpreted and large extravasations of contrast medium in the films render a study of the conditions difficult (In Figs 43 and 69 a varices are said to be present in the pelvis *whereas in reality they are superficial* varices in the superficial epigastric vein Fig 48 is stated to show the superficial circumflex iliac vein but the vessel depicted is in fact an accessory saphena magna vein with a superficial branch) *In a strikingly large* number of cases the puncture was made in the great saphenous vein or some other venous branch in the groin instead of in the femoral vein with a little practice it is nearly always possible to puncture *the latter vessel* The method described by Martinet must furthermore be considered extremely inadequate for the purpose of determining whether normal or pathologic conditions are present in the *veins of the inguinal* region In a later chapter on pelvic vein phlebography

BOOK REVIEWS

ATTAINMENT AND VALUE OF PRECISION IN DEEP RADIOTHERAPY. SOME FUNDAMENTALS WITH SPECIAL REFERENCE TO MOVING BEAM THERAPY WITH 200 TO 250 kV ROENTGEN RAYS AND COBALT 60 GAMMA RADIATION. By Olov Dahl and Karl Johan Vikterlof. 223 pages, 28 isodose charts, 90 illustrations and 25 tables. Acta radiol. (1960) Suppl. No. 189. Price Sw. Kr. 35.—

Technical development in the last two decades has consistently offered improved possibilities for radiotherapy of deep seated tumours. A high degree of accuracy throughout the radiotherapeutic proceedings is a prerequisite in the modern treatment of such tumours. This is necessary for a satisfactory application of current principles in each case and in every clinic. Moreover, since precision in all deep radiotherapy is essential for a detailed record of the method of treatment used for each clinical series, accuracy is essential for a satisfactory evaluation and comparison of biologic observations and treatment results between different clinical materials. The realization of treatment precision must therefore be regarded as equally important as detailed clinical observations in the development of radiotherapy.

The present publication is a continuation report on the work in progress for the attainment of precision in deep radiotherapy. As the recent work should be seen in its proper connection with the earlier investigations, a chronologic survey of the studies is first presented with a recapitulation of the basic principles and a general review of the results reported in our earlier publications. The work was concerned mainly with two forms of moving beam therapy, namely, perpendicular axial rotation therapy and perpendicular axial arc therapy.

Access to suitable anatomical phantoms was found to be necessary, and series of such models were constructed, appropriate regard being given to the anatomical and radiophysical factors involved. In the case of the thorax phantoms both some inadvertencies in the anatomical descriptions given in text books as well as the radiophysical properties of the functioning human lung had to be taken into consideration. As no consistent data on the radiophysical properties were available, it was first found necessary to determine them experimentally. Lungs from human cadavers inflated to a positive pressure were employed in such a manner as to ensure that physiologically adequate conditions be attained. Radiophysical determinations of the density were carried out, and, by means of corrections for divergences in blood content, a value of the average density of the functioning human lung was obtained. In further measurements a suitable lung substitute was found by means of which depth dose studies could be performed.

Since the standard isodose charts measured in homogeneous phantoms, which were presented earlier for perpendicular axial arc therapy, were intended for use in clinical practice, it was of interest to determine to what extent such dose distributions were valid in corresponding anatomical phantoms. These investigations were performed with both 200 kV roentgen rays and cobalt 60 gamma radiation and with thorax and pelvis phantoms. In these, those levels were selected that were characterized by an extreme radiophysical inhomogeneity due to the presence of pulmonary or bony tissue.

Twenty eight arc therapy dose distributions from the measurements in anatomical phantoms, judged as appropriate for direct clinical use under certain conditions, were selected. They are mainly valid for body regions of extreme radiophysical inhomogeneity, where the prognostication of the resultant dose distribution is most difficult. This means that the majority refer to the thorax region when using 200 kV roentgen rays.

A special comparison of dose distributions between 200 kV roentgen and cobalt 60 gamma irradiations with special reference to arc therapy was made. This was to evaluate further the advantages and limitations of the two radiation qualities for different clinical purposes.

worked independently and that all parts of the subject are not equally well represented Because of the large number of conference papers a strict selection was necessary but the editors seem to have made a wise choice and covered all important matters without un necessary duplication Some important points from papers which could not be included are gi en in short introductions to the various chapters

The contents range from international and national protection recommendations the experimental basis for decisions on maximum permissible levels and the experiences on per sonnel doses in practical working conditions to studies of water movements in deep sea trenches with a view to the advisability of using these trenches as permanent disposal places for fission products from large scale atomic energy work a question answered in the negative Many papers concern various dose measuring instruments and methods among which measure ments in humans and on foodstuffs of weak activities from nuclear weapons tests fall-out and other sources and the movements of activity in the soil plant animal chain command special interest Some papers consider the hazards due to alpha emitters and methods for their safe handling The bearing of meteorologic and geologic factors on the hazards from nuclear energy plants in normal operation and the possible consequences of a major disaster are also discus sed Regarding this the experiences with ground disposal of fission products at Hanford and Savannah River and the extensive survey measurements after the Windscale incident are valuable

This by no means complete survey of the contents will suffice to show the size of the circle of readers to which the present volume should appeal

Sten Benner

RADIOLOGIC EXAMINATION OF THE SMALL INTESTINE By Rose Golden 2nd edit 560 pages and 1.6 illustrations Charles C Thomas Springfield Ill 1959 Price $ 18 50

As stated in the preface to the present second edition of this work the purpose is to continue the assembling of information which seems to be helpful in understanding the significance of the roentgen examinations of the small intestine Since the first edition was published much new work on the small intestine has appeared and additional information concerning its anatomic structure and physiology has become available The author s experience since 1928 has still further increased and the second edition offers the reader all the latest knowledge of value

A general introduction the anthropology anatomy and physiology of the small bowel and the normal small intestine on radiologic examination fill up the first 75 pages of the book Conditions of developmental origin of the small intestine of the infant are then thoroughly discussed Effects of certain drugs and food on the small intestine are also touched upon Functional and organic disorders of the intestine including ileus and the use of the Miller Abbott tube are treated in detail Allergy and disorders of nutrition inflammatory diseases and neoplasms are some of the more important sections The small intestine after operation and parasitic infestation are the subjects of some other chapters All these together with some remaining chapters on various subjects form a comprehensive and concentrated treatise on this portion of the alimentary tract

The illustrations are almost uniformly of high quality and are well chosen

This is a textbook of a fundamental nature not too easy to read but thought provoking with its references to modern physiology neurology and digestive chemistry With the in creasing importance of gastro-enterology this book constitutes a basis for further studies

Ove Mattsson

written by the authors themselves the illustrations are, on the other hand, excellent and their interpretations correct

Twelve chapters are concerned with different abnormal conditions The authors own phlebograms used as illustrations in these chapters are for the most part exceedingly good but unfortunately, on pages *129* and *130*, schematic drawings of so called valveless vein sinuses in the soleus muscle taken from works by Cockett, have also been included the authors still consider that such vein sinuses may be present normally Actually, these dilated valveless veins in the calf muscles are always pathologic and should be called muscle varices

Pathologic communicating veins are rightly given much space Their sites of predilection are described and their significance in primary and secondary varices is thoroughly discussed and illustrated by diagrams and instructive phlebograms Malformations and anomalies in the venous system are treated more summarily but are also illustrated by a few of the authors own cases

Injuries to deep veins caused by injection therapy are described in a special chapter The authors over a period of 3 years watched 36 patients who had previously received injection treatment for varicose veins at other hospitals before the treatment these patients had been without symptoms but afterwards their legs became swollen and post thrombotic in appearance The damage to the deep veins is illustrated by phlebograms and good photographs showing the clinical picture This chapter should serve as a warning against the incautious use of injection therapy The most common forms of varicose vein recurrence after a previous surgical intervention are also treated clearly and instructively

The authors have devoted a special section to their own contributions to phlebography namely experimental thrombosis (in rabbits) and a description of the so called vein spur in the common iliac vein This spur is however only illustrated by drawings and it would hardly be unreasonable on the part of readers to demand that in a book on phlebography the so called vein spur given so much space in the work should be presented phlebographically

A list of references accompanies each chapter but many inaccuracies and mistakes are to be found in them On page *21* a woman investigator of the name of Birch is cited only by her Christian name Carroll and in a reference to the same work immediately afterwards the date is given incorrectly On page 119 the figures 162 (1921) 71 should be placed opposite the important work by Magnus while the data given actually refer to Lenggenhager s publication on the same page Numerous errors of this kind occur and in a work of this class ought to have been eliminated by more careful proof reading

The work is an Ergänzungsband to Fortschritte auf dem Gebiete der Röntgenstrahlen and the typography as is usual with publications from Thieme Verlag is of a very high standard Even in its present form it has a mission to fill in increasing our knowledge of phlebographic problems but in new editions there is room for considerable improvement especially as indicated in the present review

Ike Cullmo

HEALTH PHYSICS Volume I Progress in Nuclear Energy Series XII Editors W G Marley and K Z Morgan 602 pages Pergamon Press Oxford 1959 Price £ 5 5 s

Health physics is an important but ill defined subject a borderland between many natural and medical sciences The contents of this volume are therefore varied and this as well as the large number of authors preclude a review in the ordinary sense It should however be said from the very first that the book is most valuable as giving a comprehensive view of the state of the subject at the time of the Geneva Conference of 1958 It follows from the nature of things that the picture presented is somewhat disjointed as the contributors have mostly

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Ove Mattsson

DIE STREIFENATELEKTASEN DER LUNGE Von Friedrich Heuck 108 Seiten und 64 Abbildungen Georg Thieme Stuttgart 1959 Price DM 32

This book begins with a review of how striated atelectasis has been interpreted in roentgen films since 1928 This is followed by a chapter on general roentgen aspects and one on the mode of origin of atelectasis The author then describes his observations in animal experiments that mainly consisted in histologic examinations of the lungs after irritation of cervical nerves at their point of exit after irritation of the vagus nerve in the neck and after an intrapleural acetylcholine injection Other experiments in animals to ascertain the contractility of the unstriated muscle tissue at the periphery of the lungs are also described, and the author finally gives an account of findings in the surface of the lungs obtained with an intravital microscope The following conclusions were drawn from these experiments Zur Enstehung einer Streifenatelektase ist also weder ein Bronchusverschluss noch eine Kontraktion der Lungemuskulatur die in ihrer funktionellen Bedeutung umstritten ist erforderlich Wie aus meinen Untersuchungen hervorgeht, darf bei der Genese einer Streifenatelektase die vaskulare Komponente — also die Durchblutungsstorung — gegenuber der Beluftungsstorung (Bronchusverschluss nicht unterschatzt werden

The section dealing with the animal experiments will not be discussed in this review On the other hand anyone with even the slightest experience of roentgen examinations must disagree with the author s interpretation of the roentgen films of human lungs He considered he could distinguish in the actual atelectatic area an air conducting bronchus as an Aufhellung innerhalb der Verschattung These bronchi which are marked with arrows and with accompanying sketches of the air in the brohchus extend out almost to the surface of the lung! The bronchographic views intended to demonstrate the absence of any bronchial obstruction are not convincing

Uno A T Norlin

ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE, NORVEGIAE ET SUECIAE

VOL 55 APRIL 1961 FASC. 4

6

DEFORMATION OF THE RECTO SIGMOID JUNCTION IN PELVIC ENDOMETRIOSIS

by

GEORG THEANDER and LENNART WEHLIN

External endometriosis is a fairly common condition characterized by the extrauterine growth of endometrial tissue or possibly metaplastic tissue resembling endometrium Circumscribed tumefactions may develop (endometriomas chocolate cysts), but more often the process invades contiguous tissues with the formation of almost pathognomonically firm and rigid adhesions as well as a marked degree of puckering and scarring The pelvic peritoneum recto vaginal septum rectum and sigmoid colon are clinically important sites of predilection Despite the infiltrative mode of growth the mucosa of the rectum and sigmoid is however seldom invaded and rectal bleeding is therefore rare

Clinical and roentgenographic examinations are often insufficient to establish the diagnosis pre operatively Pelvigraphy may reveal membranous adhesions or obliteration of the recto uterine fossa but the findings are seldom conclusive Roentgen examination of the bowel may disclose endometriomas of this organ as well as any constrictions resulting from the more diffuse type of growth but such lesions may be difficult to distinguish roentgenographically from true neoplasms or inflammatory conditions LILJA s observation (JOSEFSSON 1939) of an increase in the strangulating effect of endometriosis on the bowel during the menstrual period is important in this respect, unfortunately however the sign seems to be demonstrable only exceptionally Despite the in

From the Roentgendiagnostic Department (Director Prof Solve Welin) Malmo Allmanna Sjukhus Malmo Sweden Submitted for publication 4 August 1960

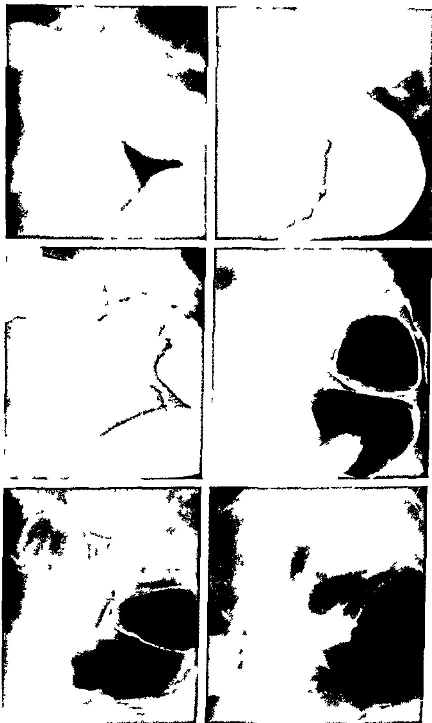


Fig 1 Deformity of recto sigmoid junction in 6 women with pelvic endometriosis Lateral views



Fig 2 Primary carcinoma at recto-sigmoid junction in 4 patients Lateral views Deformity somewhat similar to that in figs 1 and 3 but with mucosal infiltration

creasing roentgenologic interest in endometriosis of the colon and rectum (JENKINSON & BROWN 1943 CULVER & CALDWELL 1951, WIETERSEN & BALOW 1957 BOLES & HODES 1958, CULVER PEREIRA & SEIBEL 1958, SPJUT & PERKINS 1959) it is still widely believed that the roentgen appearances of the condition are uncharacteristic and of little help in establishing the diagnosis in clinically doubtful cases

A peculiar deformity of the recto-sigmoid junction is sometimes present in pelvic endometriosis and is as a rule demonstrable only in the lateral view (Figs 1 and 3) It affects the anterior wall of the bowel below the sacral promontory or to be precise, at the level of or closely above the superior rectal valve It appears as a blunt transversal ridge, about 2 to 4 cm in breadth which projects backwards into the lumen and thus seems to exaggerate the normal bend of this part of the wall The ridge is rounded and more or less distinctly demarcated in profile, but as a rule its surface is not quite smooth, one or more

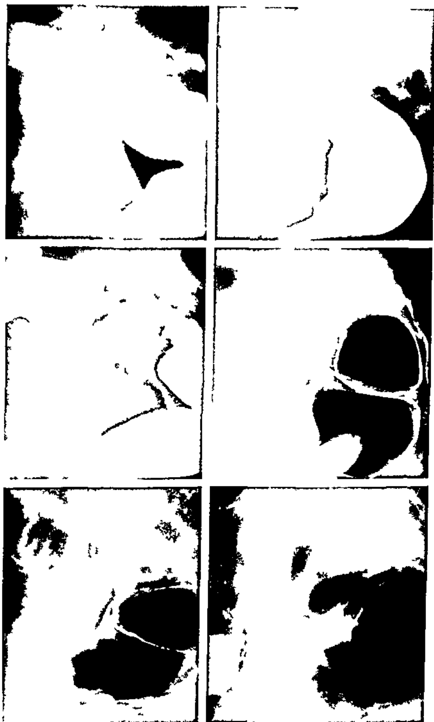


Fig 1 Deformity of recto sigmoid junction in 6 women with pelvic endometriosis Lateral views



a



b

Fig 4 Same case as in fig 3b at operation (a) and postoperatively (b) a) Folding of bowel wall and contracted adhesions traversing recto-sigmoid junction b) Persistence of deformity Metal clips at recto-sigmoid junction and in recto-uterine fossa.

to a few cysts the size of a pin head in the pelvic serosa A circumscribed endometrioma at the recto sigmoid junction was found in 2 cases only In 4 of the 6 patients with the deformity the bowel was examined roentgenographically after the operation which included salpingo-oophorectomy on one or both sides as well as supravaginal amputation or total removal of the uterus in all cases but one In one of the 4 cases small excisions of tissue were also made from the bowel wall at the recto-sigmoid junction in this case but not in the others, the deformity was absent postoperatively though the main part of the recto sigmoid infiltrate had not been removed

The deformity was extremely less common in patients without known endometriosis Of the 357 patients with primary carcinoma of the bowel the neoplasm was situated at the recto sigmoid junction in 53, but only 4 of them presented a deformity somewhat similar to that observed in pelvic endometriosis (Fig 2) In these the true nature of the condition was apparent from mucosal infiltration in the deformed segment of the bowel wall Two of the remaining 340 patients studied showed the deformity under consideration One of them (Fig 3a) had been treated with bilateral salpingo-oophorectomy and radio therapy for an ovarian carcinoma the deformity was absent pre operatively but appeared during the postoperative course with the development of a tender retro-uterine tumefaction In the other patient (Fig 4) the deformity was caused by an inflammatory reaction of the pelvic peritoneum to a condition of terminal ileitis At operation firm adhesions covering the anterior



Fig 3 Deformity of recto sigmoid junction in lateral views after removal of ovarian carcinoma and radiotherapy (a) and in terminal ileitis with pelvic adhesions (b)

small wrinkles may be seen to continue laterally and dorsally as transverse folds of the bowel wall The ridge is resistant to any attempts to distend the bowel by instillation of contrast medium or insufflation of air, and it usually prevents passage of a sigmoidoscope Since the deformity seems to have received little attention in the literature, a study of its occurrence and significance was thought to be of interest

Material and Method The study was based on observations made in 8 women with pelvic endometriosis, 176 women and 181 men with primary carcinoma of the bowel, and 169 women and 171 men selected at random from patients admitted for various reasons but not known to have carcinoma of the bowel or endometriosis In all of these 705 patients the bowel had been examined roentgenographically at least once, and then with few exceptions with the double contrast method used as a routine in our department (ANDREN, FRIEBERG & WELIN 1955, ANDREN & FRIEBERG 1956) The films taken at those examinations were re examined for the peculiar deformity described above, and essential clinical and histologic data were extracted from available records

Results

The deformity under consideration was present in 6 of the 8 women with pelvic endometriosis (Fig 1) In these 6 and in one of the others operation revealed firm adhesions of pelvic structures including the uterus and the anterior surface of the bowel, whereas in the remaining case the lesions were limited

As a matter of fact firm adhesions and transversal folding of the bowel wall at the recto sigmoid junction were observed at operation in the case of terminal ileitis included in the present material (Fig 4a) Judging from an illustrative diagram given by HULTBORN, MORALES & ROMANUS similar findings were made by them in the man with pelvic metastases *from a pancreatic carcinoma* referred to above In pelvic endometriosis the tendency of the adhesions to undergo fibrosis and to contract is conspicuous and has been pointed out by *many authors even* the consequent folding and angulation of the bowel wall has been observed (TAGART 1959)

The assumption that the deformity is due to contraction of recto-sigmoid adhesions would explain the roentgenographic appearances of the deformity as well as its location and common occurrence in pelvic endometriosis It would also explain the disappearance of the deformity after incision of the anterior wall of the affected segment of the bowel as observed in one case *reported above If dependent on* mucosal folding as we have presumed, the deformity will be absent in spite of abundant pelvic adhesions if the latter do not contract sufficiently or if their longitudinal fibres are cut

In view of the above observations other pathologic conditions causing contracting adhesions in the pelvis e g, fibrosis following infections or radiotherapy must also be considered in the establishment of a differential diagnosis However the most important task of the roentgenologist is to distinguish the *deformity from infiltration caused by primary carcinoma of the bowel* The difficulty encountered in this decision is emphasized by the fact that in 4 of our cases the deformity caused by endometriosis was first erroneously believed to be due to a primary carcinoma Review of the 357 cases of the latter disease included in the present study strengthened, however our opinion that a technically satisfactory roentgen examination of the bowel will practically always provide sufficient information for a correct diagnosis

SUMMARY

The recto-sigmoid junction was studied roentgenographically in 703 cases to determine the diagnostic significance of a deformity observed in that part of the bowel in 6 out of 8 cases of pelvic endometriosis Contraction of serosal adhesions appeared to be responsible for the development and the characteristic appearance of the deformity

ZUSAMMENFASSUNG

Die Gegend des Überganges vom Rectum zum Sigmoideum wurde in 703 Fällen röntgenologisch studiert um die diagnostische Signifikanz einer Deformität festzustellen die bei 6 von 8 Fällen mit Beckenendometriose in diesem Darmabschnitt beobachtet worden ist Kontraktion von Serosaadhäsionen schienen für die Entwicklung und das charakteristische Aussehen der Deformität verantwortlich zu sein

surface of the bowel at the recto sigmoid junction were found to keep this part of the bowel wall in a state of rigid puckering with fixed transverse folds (Fig 4a) There was no obliteration of the recto uterine fossa, and the position of the recto genital septum was definitely lower than that of the recto sigmoid junction To facilitate orientation on subsequent roentgenographic examination, metal clips were fastened at the recto sigmoid junction and in the floor of the recto uterine fossa On re examination 4 weeks after operation, the deformity of the bowel wall was still demonstrable (Fig 4b)

Discussion

It is apparent from the present material that the deformity of the recto sigmoid junction under consideration is fairly characteristic in women with pelvic endometriosis but not pathognomonic of this disease Several kinds of pathologic processes outside the rectum may deform this organ at various levels by causing a ridge shaped protrusion of part of its wall into the lumen Ever since the description by BLUMER (1909) of such protrusions as 'rectal shelfs', the condition is usually referred to as a 'shelf tumour irrespective of its actual nature In women it is most often due to various lesions of the genital system (BUIL, JACKMAN & VICKERS 1941)

HULTBORN, MORALES & ROMANUS (1955) published a roentgenographic study of the rectum in 11 patients with a 'shelf tumour including 3 women in whom the condition was caused by pelvic endometriosis involving the rectal wall No distinction was made by these authors between the different types of deformity observed, but, judging from the illustrations and descriptions given, the recto sigmoid junction presented the abnormal shape under discussion in at least 2 of the 3 women mentioned and probably also in one man with pelvic metastases from a pancreatic carcinoma The factor essential for the development of the 'shelf tumour was thought to be a pathologic fixation of the uppermost part of the recto genital septum rendering possible a backward protrusion of the anterior rectal wall by this structure Since, however the septum in one of our cases was not at the same level as the deformity (Fig 4b), this explanation for the 'shelf' does not seem to be valid The deformity under discussion would appear to be more likely due to fibrous contraction of adhesions at the recto sigmoid junction

In general, shrinkage of tissue covering any segment of the bowel must inevitably result in permanent folding of the part of the bowel wall adherent to such tissue If only, or mainly, the anterior wall is affected, the longitudinal component of the contraction will probably be predominant and give rise to a forward bending of the wall as well as a transverse arrangement of the resultant folds Such a course of events is apparently favoured by the anatomic conditions characteristic of the recto sigmoid junction, namely, an anterior curvature and a limitation of the serosal covering to the anterior surface

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Les auteurs ont étudié radiographiquement dans 705 cas la jonction recto sigmoïdienne pour déterminer la valeur diagnostique d une déformation de cette partie de l intestin observée dans 6 cas sur 8 d endométriose pelvienne C est la rétraction d adhérences péritonéales qui paraît être la cause de l apparition et de l aspect caractéristique de cette déformation

REFERENCES

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— — and WELIN, S Roentgen diagnosis of small polyps in the colon and rectum Acta radiol 43 (1955) 201

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RADIOLOGIC EVALUATION OF FUNNEL CHEST

by

OLE G BACKER, S BRUNNER and V LARSEN

An assessment of the amount of depression of the sternum in funnel chest is generally based either upon the depth of the funnel or upon the minimum distance between the vertebral column and the posterior surface of the body of the sternum Since however, the majority of the patients subjected to operation are children absolute measurements are inapplicable in analysing the late results of the corrective procedures

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Fig 1 Lateral view of patient with moderate funnel chest Arrows indicate the measurements used in calculating the vertebral index

Control series

The normal range of these indices and their relation to sex and age were studied in a normal series of 197 males and 248 females, a total of 445 subjects, almost equally distributed in the 5 year age groups from 0 to 25 years

Fig 2 gives the distribution of the fronto sagittal index in the total normal series The mean value and dispersion were calculated for each one year age group The variation around the solid average curve is illustrated by the two broken lines traced at a distance of twice the dispersion The area between these two curves covers 95 % of the observations As no significant sex differences were found, the series were considered together The index fell abruptly during the first 5 or 6 years of life after which it remained practically unchanged around a mean value of about 16, throughout the remainder of the growth period

Fig 3 shows the corresponding distribution average curve, and 95 % range of the vertebral index in the total normal series There was no significant sex difference During the first 6 years of life the index increased perceptibly, after which it remained at about 20 throughout the remainder of the growth period

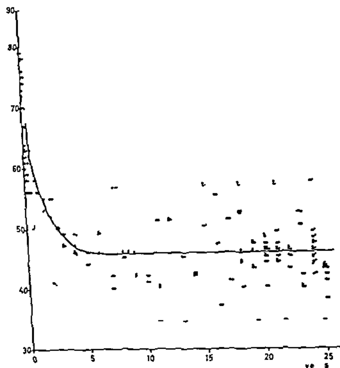


Fig 2 Fronto-sagittal index in the normal series (445 subjects) The solid line represents the mean curve The 95% range lies between the broken lines

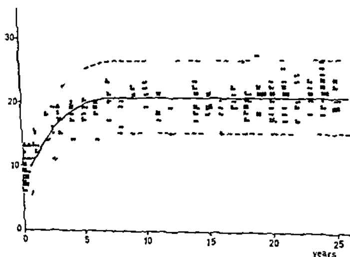


Fig 3 Vertebral index in the normal series (445 subjects) The solid line represents the mean curve The 95% range lies between the broken lines

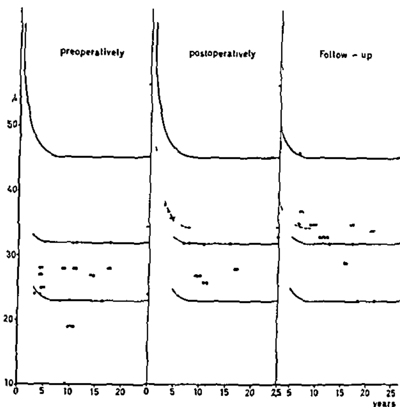


Fig 4 Fronto sagittal index for the operation series pre operatively post operatively and at follow up The normal values are indicated by the mean curve and the 95 % range The two curves at the bottom indicate the severity of the funnel chest From bottom to top severe moderate and mild cases

Practical application

The applicability of the indices was tested and their relation to the absolute measurements was fixed in a series of 74 patients operated upon for funnel chest during the period 1948—1958 and followed up for an average of 4 2 years (0 8 to 10 3 years)

In funnel chest the fronto sagittal index is below normal and the vertebral index above normal After reduction of the sternum the two indices show a rise and a fall respectively Where the primary operative result is good, the indices are brought within the normal ranges A recurrence manifests itself in a renewed fall in the fronto sagittal index and a rise in the vertebral index, as compared with the values found immediately after the operation

Figs 4 and 5 set out the indices in the series of patients with funnel chest, before operation, immediately following operation, and at follow up The normal average curve and the 95 % ranges are plotted in the figures

The correlation between the percentage increase in the sterno vertebral distance and changes in the two indices are shown in Figs 6 and 7

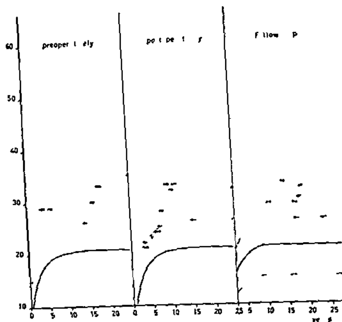


Fig 5 Vertebral index in the operated series pre-operatively postoperatively and at follow up Normal values indicated by the mean curve and the 95 range

The normal average distance from the vertebral column to the sternum is considered to be about 10 cm in adults (according to ROESLER 10 3 cm in males and 9 2 cm in females) According to FABRICIUS et coll a funnel chest in an adult is severe if the distance between the vertebral column and the sternum is 5 cm or less and moderate if this distance is between 7 and 5 cm The corresponding border line values of the fronto sagittal index may be deduced on this basis The material was divided into 28 severe 35 moderate, and 7 mild cases by plotting in Fig 4 two curves parallel to the normal average curve, with ordinates of 50 % and 70 % respectively One case fell within the normal range

The secondary results of operation in the 74 operated cases are summarized on p 255 It may be seen that 20 (27 %) were unchanged or worse 28 (38 %) were corrected to within the normal range and the remaining 26 cases (35 %) were markedly improved Furthermore it appears that the results were most satisfactory in cases of severe funnel chest Of 28 severe cases 25 were improved while in 3 the condition postoperatively was unchanged (11 %) Among the moderate and mild cases no improvement occurred in 31 % and 71 % respectively

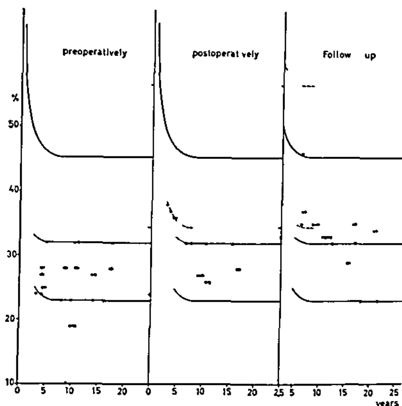


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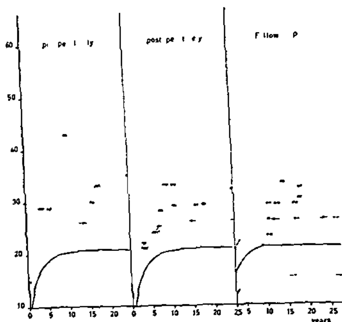


Fig Vertebral index in the operated series pre-operatively postoperatively and at follow up Normal values indicated by the mean curve and the 95 range

The normal average distance from the vertebral column to the sternum is considered to be about 10 cm in adults (according to ROESLER 10 3 cm in males and 9 2 cm in females) According to FABRICIUS et coll a funnel chest in an adult is severe if the distance between the vertebral column and the sternum is 5 cm or less and 'moderate if this distance is between 7 and 5 cm The corresponding border line values of the fronto sagittal index may be deduced on this basis The material was divided into 28 severe 35 moderate and 7 mild cases by plotting in Fig 4 two curves parallel to the normal average curve with ordinates of 50 % and 70 % respectively One case fell within the normal range

The secondary results of operation in the 74 operated cases are summarized on p 255 It may be seen that 20 (27 %) were unchanged or worse, 28 (38 %) were corrected to within the normal range, and the remaining 26 cases (35 %) were markedly improved Furthermore it appears that the results were most satisfactory in cases of severe funnel chest Of 28 severe cases 25 were improved, while in 3 the condition postoperatively was unchanged (11 %) Among the moderate and mild cases no improvement occurred in 31 % and 71 % respectively

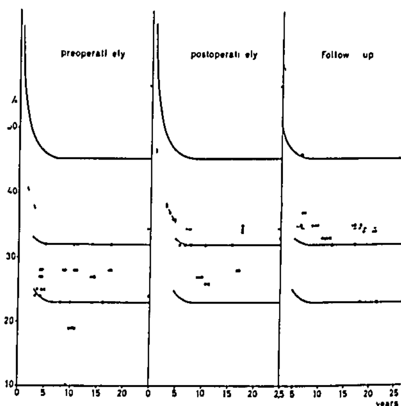


Fig 4 Fronto sagittal index for the operation series pre operatively post operatively and at follow up The normal values are indicated by the mean curve and the 95 range The two curves at the bottom indicate the severity of the funnel chest From bottom to top severe moderate and mild cases

Practical application

The applicability of the indices was tested and their relation to the absolute measurements was fixed in a series of 74 patients operated upon for funnel chest during the period 1948—1958 and followed up for an average of 1 2 years (0 8 to 10 3 years)

In funnel chest the fronto sagittal index is below normal and the vertebral index above normal After reduction of the sternum the two indices show a rise and a fall respectively Where the primary operative result is good, the indices are brought within the normal ranges A recurrence manifests itself in a renewed fall in the fronto sagittal index and a rise in the vertebral index, as compared with the values found immediately after the operation

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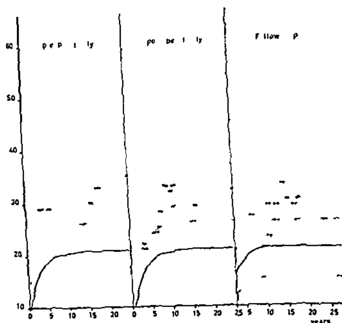


Fig 5 Vertebral index in the operated series pre-operatively postoperatively and at follow up Normal values indicated by the mean curve and the 95 range

The normal average distance from the vertebral column to the sternum is considered to be about 10 cm in adults (according to ROESLER 10 3 cm in males and 9 2 cm in females) According to FABRICIUS et coll a funnel chest in an adult is severe if the distance between the vertebral column and the sternum is 5 cm or less and moderate if this distance is between 7 and 5 cm The corresponding border line values of the fronto-sagittal index may be deduced on this basis *The material was divided into 28 severe 35 moderate and 7 mild* cases by plotting in Fig 4 two curves parallel to the normal average curve *with ordinates of 50 % and 70 % respectively* One case fell within the *normal* range

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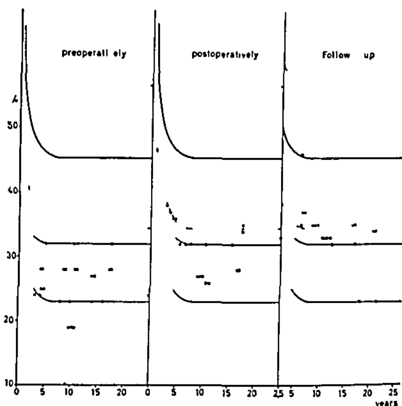


Fig. 4. Fronto-sagittal index for the operation series pre-operatively, post-operatively and at follow-up. The normal values are indicated by the mean curve and the 95 % range. The two curves at the bottom indicate the severity of the funnel chest. From bottom to top: severe, moderate and mild cases.

Practical application

The applicability of the indices was tested and their relation to the absolute measurements was fixed in a series of 74 patients operated upon for funnel chest during the period 1948—1958 and followed up for an average of 4.2 years (0.8 to 10.3 years).

In funnel chest the fronto-sagittal index is below normal and the vertebral index above normal. After reduction of the sternum the two indices show a rise and a fall respectively. Where the primary operative result is good, the indices are brought within the normal ranges. A recurrence manifests itself in a renewed fall in the fronto-sagittal index and a rise in the vertebral index, as compared with the values found immediately after the operation.

Figs 4 and 5 set out the indices in the series of patients with funnel chest, before operation, immediately following operation, and at follow-up. The normal average curve and the 95 % ranges are plotted in the figures.

The correlation between the percentage increase in the sterno-vertebral distance and changes in the two indices are shown in Figs 6 and 7.

Pre operative condition	*Secondary results*	
Severe funnel chest 28 cases	Severe funnel chest	3 cases
	Moderate » »	12
	Mild » »	2 »
	Corrected	11 »
Moderate funnel chest 35 cases	Severe funnel chest	1 case
	Moderate » »	10 cases
	Mild » »	10 »
	Corrected	14 »
Mild funnel chest 7 cases	Severe funnel chest	1 case
	Moderate	3 cases
	Mild » »	1 case
	Corrected	2 cases
Normal 1 case	Normal	1 case
No pre-operative films 3 cases	Severe funnel chest	1 case
	Moderate » »	1 »
	Mild » »	1 »

Displacement of the heart Cardiac displacement, if any is generally included in the radiologic evaluation of funnel chest This displacement may be to one side, generally the left, or in the form of rotation on various axes (vertical, sagittal horizontal and fronto-horizontal) Among the 74 patients included in the follow up 49 (66 %) had displacement of the heart to the left pre operatively Out of these 49 patients 35 had satisfactory correction of the sternum at follow up but the displacement of the heart remained unchanged in 18 In other words the heart remained displaced in half the cases even despite correction of the sternal deformity

Discussion

The increase in the absolute distance between the vertebral column and the sternum is applicable in assessing the primary result of operation for funnel chest It is inapplicable, however, in evaluating the late results since most of the patients are children The assessment of the late results has been based up to now on a subjective estimate and this has made it difficult to compare the different series

The relative measurements described are well defined in a normal series and allow objective evaluation of the primary as well as secondary results This permits a comparison within the same series at different times following operation

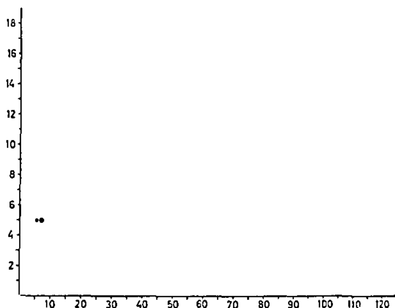


Fig 6 Correlation between percentage increase in sterno-vertebra distance (abscissa) and increase in fronto sagittal index (ordinate

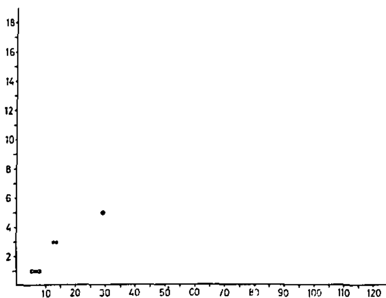


Fig 7 Correlation between percentage increase in sterno vertebral distance (abscissa) and decrease in vertebral index (ordinate)

Pre-operative condition	*Secondary results*	
Severe funnel chest 28 cases	Severe funnel chest	3 cases
	Moderate »	12 »
	Mild »	2 »
	Corrected	11 »
Moderate funnel chest 35 cases	Severe funnel chest	1 case
	Moderate » »	10 cases
	Mild »	10 »
	Corrected	14 »
Mild funnel chest 7 cases	Severe funnel chest	1 case
	Moderate »	3 cases
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Normal 1 case	Normal	1 case
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The relative measurements described are well defined in a normal series and allow objective evaluation of the primary as well as secondary results This permits a comparison within the same series at different times following operation

A prerequisite for the vertebral index is a true lateral view, even a slightly oblique projection will make the diameter of the vertebral body too large and the sagittal diameter of the chest too small, so that the index will in turn become too high

The secondary changes in cardiac configuration and in the hila of the lungs, described by previous authors (ALBRECTSEN 1954, EDLING 1953, EVANS 1946, ERNBERG 1951, FABRICIUS et coll 1957), are less suited for assessing the result of an operation upon a funnel chest because in many cases these changes persist even after satisfactory correction of the sternum This was observed in the present series and has previously been described by PALTIA et coll (1959)

SUMMARY

The primary and secondary operative results in 74 cases of funnel chest were evaluated radiologically by means of two relative measurements of the sternal depression viz a fronto-sagittal index and a vertebral index defined in a series of 445 normal subjects

ZUSAMMENFASSUNG

Die primären und sekundären Operationsresultate in 74 Fällen mit Trichterbrust sind radiographisch untersucht worden Man benutzte dabei 2 relative Messungen der sternalen Depression nämlich einen fronto-sagittalen und einen vertebralen Index welche man mit Hilfe von 445 Normalpersonen definiert hatte

RÉSUMÉ

Les auteurs ont établi sur une série de 445 sujets normaux un indice thoracique fronto sagittal et un indice vertebral permettant de mesurer la depression sternale Au moyen de ces deux mesures ils ont évalué radiographiquement les résultats opératoires immédiats et éloignés dans 74 cas de thorax en entonnoir

REFERENCES

ALBRECTSEN S R Tragtbryst (funnel chest) (In Danish) Ugeskr Læg 116 (1954), 905

EDLING, N P G The radiologic appearances of the heart oesophagus and lungs in funnel chest deformity Acta radiol 39 (1953) 273

ERNBERG T The symptom complex in cor planum Acta med scand Suppl 262 (1951) 51

EVANS W The heart in sternal depression Brit Heart J 8 (1946) 162

FABRICIUS J DAVIDSEN H G and HANSEN A T Cardiac function in funnel chest Dan med Bull 4 (1957) 251

PALTIA, V PARKKULAINEN K V SULAMAA M and WALLGREN G R Operative technique in funnel chest Acta chir Scand 116 (1959) 90

ROESLER, H Quoted by Fabricius et coll

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR PROF SOLVE WELIN), UNIVERSITY OF LUND MALMÖ ALLMÄNNA SJUKHUS, MALMÖ SWEDEN

THE DOUBLE CONTRAST METHOD IN ULCERATIVE COLITIS

by

SOLVE WELIN and FOLKE BRAHME

The last decade has witnessed an increase in interest in the diagnosis and treatment of ulcerative colitis This is to no small extent due to the introduction of new therapeutic methods and to more active surgery Experience has shown that the risk of malignant degeneration in the chronic stage of the disease is considerable and that carcinoma arising in cases of colitis is highly malignant and forms early metastases All workers in this field have been impressed by the poor prognosis In REIFFERSCHEID's compilation of 22 456 cases of ulcerative colitis only 3 5 % were found to have cancer but for those who had had colitis for 5 years or more the frequency was 17 % and for those who had had the disease for 15 years it was as high as 25 % LAGERCRANTZ found a frequency of 33 % in a paediatric series in which the children had had colitis for more than 10 years CATTELL found that in cases he had operated upon the overall incidence of carcinoma was 7 % but of those who had had the disease for 9 years or more before the operation malignant lesions developed in one third COUNSELL and DUKES gave a corresponding frequency of 45 5 % Some authors even claim that when treatment is confined to non surgical method patients with chronic ulcerative colitis undoubtedly die with undiagnosed cancer for the symptoms of a neoplasm are also those of colitis Since colectomy is said to carry an operative mortality of only 6 9 % many believe prophylactic colectomy to be justified in chronic cases An early

Submitted for publication 16 September 1960

operation may alter the natural course of this condition, and more and more clinicians are now inclined to refer their patients for operation at a relatively early stage According to SLANEY and BROOKE, total colectomy is indicated even if cancer has developed They had two patients who were alive 6 and 8 years after excision of the large bowel It is obvious that this tendency places increasing demands on diagnostic roentgenology Clinicians now wish to have definite information on the nature of any change and preferably whether or not such a change is reversible

As early as 1912 STIERLIN described the roentgenographic features of ulcerative colitis Since then many papers on this subject have been published In the beginning, barium meals and enemas were used but at that time changes could be demonstrated only if they were relatively marked Later, the examination was extended to include the post evacuation film, which gives a fair demonstration of the mucosa and therefore constitutes an essential part of the examination

Reports on the use of the double contrast method in ulcerative colitis are fairly scanty, probably because of the poor results so often obtained We have only found two authors who have recommended the method, namely FELDMAN and BACON FELDMAN in his book (1957) says that 'the double contrast enema with air insufflation of the colon is of considerable aid in the study of this condition , and BACON (1958) states that the double contrast method is an invaluable aid and is to be strongly recommended in the effort to determine the extent, the severity and the complicating factors not clearly evidenced by the mere administration of barium'

Other workers in this field express a more or less opposite opinion According to STEVENSON (1954), for example, the double contrast method will not show pathologic changes in inflammatory processes of the colon, because the air will distend the colon to its normal size and the mucosal detail will be lacking In his opinion then the method is useless PANSDORF found it difficult to cleanse the intestine properly and BUCKSTEIN stated that regarding air inflation of the colon in ulcerative colitis a word of caution is essential There is a definite tendency for these ulcers to perforate, and this tendency may be exaggerated by any effort at gaseous distention The routine use of such a procedure in this disease should therefore be discouraged, if employed at all, the method should, according to him, be applied only to cases that are well beyond the stage of acute inflammation KALIL and ROBBINS also refrain from the use of the double contrast method because of the risk of perforation They stated, however, that in those cases in which air was by chance present or had been introduced the stippling was particularly clear In 1959 DICK, BERRIDGE and GRAYSON published an extremely detailed investigation of the pathologic basis for the roentgen changes in ulcerative colitis Their material consisted of 10 patients who had undergone colectomy for ulcerative colitis These patients had also been examined by the double contrast method and on only one oc

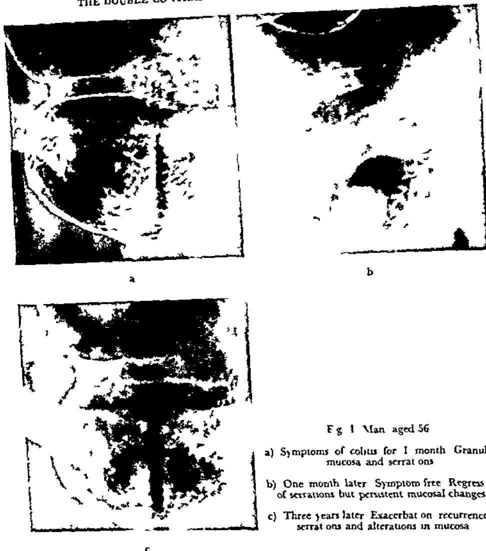


Fig 1 Man aged 56

a) Symptoms of colitis for 1 month Granular mucosa and serrations

b) One month later Symptom free Regression of serrations but persistent mucosal changes

c) Three years later Exacerbation recurrence of serrations and alterations in mucosa

casion had the method revealed changes that could not be demonstrated by barium enema or post evacuation films

Our modification of the double contrast method described in a number of previous papers has proved extremely efficient and has often yielded information that could not be obtained by previous methods The diagnosis has become more refined and more reliable and permits of a relatively early diagnosis It has also been possible to follow the course of the disease much better than previously Moreover the examination of patients with ulcerative

operation may alter the natural course of this condition, and more and more clinicians are now inclined to refer their patients for operation at a relatively early stage. According to SLANEY and BROOKE, total colectomy is indicated even if cancer has developed. They had two patients who were alive 6 and 8 years after excision of the large bowel. It is obvious that this tendency places increasing demands on diagnostic roentgenology. Clinicians now wish to have definite information on the nature of any change and preferably whether or not such a change is reversible.

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Fig 3 Male aged 16 Pseudopolyposis in the descending colon with fairly deep ulcerations



Fig 4 Woman aged 5? Deep ulcerations in transverse colon in places causing a double outline Pseudopolyposis

It has long been known that the inflammatory process may start anywhere in the colon and that in some forms of ulcerative colitis proctoscopy shows nothing pathologic In such cases only roentgen examination may verify the clinical suggestion According to the American literature colitis is localized beyond proctoscopic reach in 8 to 10 % of all cases In our series the corresponding figure was found to be 13 % From a pathologic point of view the process begins with hyperaemia and oedema of the mucosa and can be demonstrated by our method It appears that the indenture sign described by POPPEL and BERANBAUM represents a later stage with more advanced mucosal alterations even though the authors claim that it is not due to ulcerations but only represents barium extending in between the rather uniformly swollen mucosal folds The small mucosal changes demonstrated by the present method are also seen in exacerbations and remissions in patients with slight ulcerations They will not be visible in barium enema or postevacuation films because the changes are too small

It is probable that these early cases are responsible for the previous discrepancy between the clinical picture and the roentgen findings it having often been claimed that the roentgenographic appearance has been normal



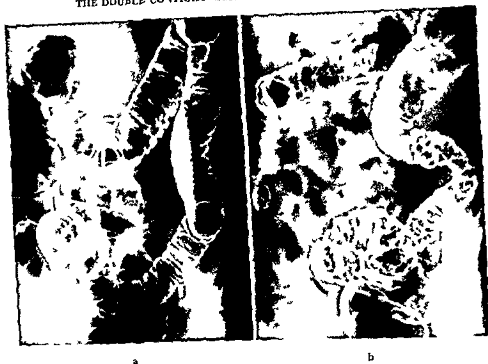
a b

Fig 2 Woman aged 65 a) Slight mucosal changes in rectum Incipient pseudopolyposis of sigmoid with ulcerations b) 4 months later No symptoms Total regression in rectum, no ulceration in sigmoid but still changes in the mucosa

colitis has never produced any complications, and the slight irritation some times occurring in association with the examination is often followed by a period of several weeks during which the symptoms are less severe than before the roentgen examination This might possibly be explained by the tannin in the Clysodrast preparation and possibly also by the barium One case of acute exacerbation in association with the examination has, however, been observed We have used the double contrast method routinely since the autumn of 1953 in more than 15 000 cases

We have modified the preparation of patients with known ulcerative colitis Patients with an acute exacerbation of their colitis or with colitis in an acute stage no longer receive castor oil the day before the roentgen examination, and usually no cleansing enema Clysodrast is not added to the enema given on the day of the examination but incorporated in the two barium enemas, the first of which extends up to the proximal aspect of the splenic flexure and the other to about the middle of the sigmoid colon All patients receive 1 mg of atropine half an hour before the examination

From November 1953 to September 1960 we have found changes suggestive of ulcerative colitis in 160 patients in most of whom the diagnosis was con firmed on proctoscopy, operation or postmortem examination The diagnosis has, however, not been verified in a few of the unoperated cases in which the ulcerative changes were localized to regions beyond the reach of the proctoscope



a b

Fig 6 Man aged 47 Periodic diarrhoea since 1930 a) Normal roentgenogram b) 15 years later Pseudopolyposis with several ulcerations stenosis of ascending colon and caecum

the rectum had a normal appearance (Fig 2b) Proctoscopic examination revealed no signs of a pathologic condition

Ulcerations may develop in the somewhat more advanced cases in which the inflammatory process is no longer localized to the mucosal surface but has penetrated deeper into the intestinal wall In the beginning they appear as pinpoint to pinhead sized tiny serrations along the edge of the bowel (Fig 1a) These are miliary abscesses which on breaking down produce small ulcers KALIL and ROBBINS in particular, stressed the importance of these roentgen findings as an early sign of ulcerative colitis

If the process progresses it will result in a deepening and widening of the ulcers (Fig 3) The ulcers may remain limited by the muscularis or they may penetrate through it to form a submuscular abscess giving the collar stud appearance If the ulcerations continue to increase in size and particularly in number they may cause a double outline in the roentgenogram (Fig 4) According to KALIL and ROBBINS this is due to a large number of such deep ulcers the inner wall being outlined by the mucosa the outer wall by barium contained in the bases of the deep ulcers DICK BERRIDGE and GRAYSON,



Fig. 5. a) Boy aged 13. Pseudopolyposis of sigmoid, rectum not involved. b) Man aged 65. Massive pseudopolyposis in rectum and sigmoid.

in clinically definite cases of ulcerative colitis with positive proctoscopic findings. In RICKETT's material, for example, there was an apparently normal colon on roentgen examination in 60 of 156 patients with clinical evidence of non-specific ulcerative colitis. They explained this by the assumption that the condition may remain a relatively superficial process in many cases with symptoms of long duration. In this connection it might be pointed out that the diagnosis of ulcerative colitis cannot be established roentgenologically unless actual ulcerations can be demonstrated.

We have been able to demonstrate the early change in the mucosa in as many as 23 patients and we have found this refinement of the method to be of great importance. The double contrast film shows a somewhat irregular finely granular surface (Fig. 1). When the disease was localized to the rectum, proctoscopy revealed a somewhat swollen mucosa with a certain tendency to bleeding. The granulation in the mucosa is sometimes coarser and more marked. This may then give the impression of incipient pseudopolyposis and the demarcation between the changes in this stage and the initial stage is vague. This is illustrated in Fig. 2a in which the changes are somewhat more advanced in the sigmoid colon, which also contains ulcerations, than in the rectum. These findings were confirmed on proctoscopy. After 4 months' treatment, during which all symptoms disappeared, roentgen examination showed a considerable regression of the changes. The ulcerations in the sigmoid had by then completely disappeared, only a certain granulation persisted while

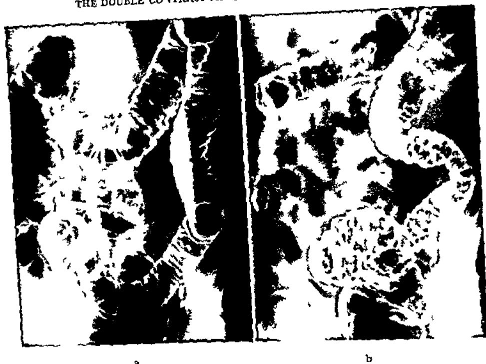


Fig 6 Man aged 42 Periodic diarrhoea since 1930 a) Normal roentgenogram b) 1 5 years later Pseudopolyposis with several ulcerations stenosis of ascending colon and caecum

the rectum had a normal appearance (Fig 2b) Proctoscopic examination revealed no signs of a pathologic condition

Ulcerations may develop in the somewhat more advanced cases in which the inflammatory process is no longer localized to the mucosal surface but has penetrated deeper into the intestinal wall In the beginning they appear as pinpoint to pinhead sized tiny serrations along the edge of the bowel (Fig 1a) These are miliary abscesses which on breaking down produce small ulcers KALIL and ROBBINS in particular stressed the importance of these roentgen findings as an early sign of ulcerative colitis

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a b

Fig 7 Woman aged 25 Symptoms of colitis for 4 months a) Granular mucosal relief in transverse colon and serrations b) 2 months later Clinical improvement but pseudopolyposis and deeper ulcerations

who compared the histologic and roentgen findings, found that the double contour is associated with active acute inflammation in which there are islands of inflamed mucosa interspersed with denuded ulcerative areas The change, demonstrated best by the double contrast method, is probably pseudopolyposis The method gives much more reliable information than any other on the extent and severity of the lesions The pathologic basis in the severe, acute phase is said to be islands of non ulcerated swollen mucosa between deep ulcers, in the chronic stages fibrous tags remain after destruction In double contrast films the changes appear as a mottled honeycombed and marbled pattern because of the numerous small, rounded formations projecting into the lumen Pseudopolypi may vary considerably in size (Figs 3, 5a and 5b) *and we have often found it hard to distinguish between granular mucosa* and pseudopolyposis

Some authors claim that it is sometimes difficult to make a differential *diagnosis between pseudopolyposis and adenomatosis* HAWKES and SHIELD state, however, that such a differential diagnosis is possible by barium enema examination since cases with pseudopolyposis have lost haustration and have *luminal stenosis and mucosal thickening with segmental involvement* of the bowel, while in adenomatosis haustration of the colon is normal and there is no stenosis Since the introduction of the double contrast examination we *have had no difficulty in differentiating between the two conditions* In this material we have diagnosed pseudopolyposis in 23 patients, or in 14 % BARGEN gave a figure of 10 % How quickly pseudopolyposis can develop is illustrated *by the following* 2 cases

Case 1 Man aged 42 referred for roentgen examination of the large bowel because of rectal bleeding this showed no evidence of abnormality (Fig 6a) Proctoscopy revealed a readily bleeding mucosa which was *however not swollen Because of recurrent symptoms*



Fig 8 Woman aged 24 with symptoms of colitis for 10 years Typical appearances in chronic stage



Fig 9 Woman aged 46 Dilatation of descending colon and stenosis of rectum

of colitis the patient was re examined roentgenologically 18 months later and advanced changes were seen in the form of pseudopolyposis and deep ulcerations in the sigmoid and the descending and transverse colon with shortening and marked stenosis of the ascending colon and caecum (Fig 6b)

Case 2 Woman aged 25 who after periods of diarrhoea with a passage of 4 to 5 stools a day for 4 months was referred for roentgen examination A double contrast examination showed that the mucosa of the transverse colon here and there was slightly granular and contained numerous small ulcerations (Fig 7a) The patient responded well to antibiotics and steroids and the symptoms abated considerably Roentgen examination two months later however revealed deeper lesions and severe pseudopolyposis in the same regions The process had now also involved the descending colon (Fig 7b)

Double contrast studies will also give a good impression of the condition of the intestinal wall in the chronic healing stages of the disease in patients with only slight symptoms The mucosa is often atrophic (Fig 8) The classical changes with shortening of the intestine straightening of the flexures, stenosis of the lumen and absence of haustration are also generally evident

LUMB PROTEROE and RAMSEY stress that colonic dilatation is sometimes seen This dilatation may be general but in some cases is localized to one segment They emphasize the recognition of dilatation of the colon as attending fulminating ulcerative colitis and RIFSTEIN inclines to the view that a distended



Fig 10 Woman aged 38 Complicating fistulae with abscess



Fig 11 Man aged 28 Granular mucosa and cancer of descending colon

segment of the colon, without small bowel distention, is a sign of impending perforation

Our series also included such a case of dilatation The patient had only slight symptoms at the time of the examination, the clinician who had referred the patient for examination believed the disease to be in the healing stage Examination, however, revealed (Fig 9) considerable dilatation of the sigmoid and descending colon and the aboral segment of the transverse colon, while the rectum was narrowed The examination also showed numerous polypous formations, the largest of which were situated in the descending colon

Practically all authors stress the risk of perforation and formation of fistulae Our examination method should demonstrate such changes, and in several cases we have been able to distinguish short fistulae from deeper ulcerations The fistulae sometimes assume considerable proportions (Fig 10)

Malignant degeneration is one of the most serious complications of ulcerative colitis, and is also one of those that has received most space in the literature There appears to be general agreement that this coincidence is of a causal nature and not simply due to chance There is evidence that the degeneration develops more often in children who have ulcerative colitis and at an earlier stage in patients with ulcerative colitis than in those not so affected Cancer usually sets in within a phase of the ulcerative colitis that may be described

as a healing stage, but it is still debatable whether the malignant process arises from an atrophic mucosa pseudopolyposis or in association with malignant degeneration of a polyp EDLING et coll state that polyposis, pseudo polyposis or pseudopapillomatosis were certainly not demonstrated in all their cases of cancer and they stress that they do not consider that cancer in ulcerative colitis is usually preceded by the formation of polypi JOHNSSON and ORR believe that the pseudopolypoid tumours that occur never become true polypi and that they may even regress and disappear According to SPRATT, ACKERMAN and MAYER pseudopolypi of ulcerative colitis cannot give rise to carcinomas because except at their periphery they lack epithelial cells

FELSEN and WOLARSKY had previously concluded that this complication developed independently owing to pre existing adenomas, and COUNSELL and DUKES who found cancer in 13 of 63 specimens of the colon in cases of ulcerative colitis made the observation that the malignant lesions often display none of the usual gross features of neoplasm of the bowel, and that malignant cells commonly lurk in strictures with no macroscopic characteristics

Our series included only 4 cases with malignant degeneration Two of them had had signs of colitis for 7 and 20 years respectively acute ileus was the indication for roentgen examination in one and in the other case a primary tumour was suggested because of the accidental finding of carcinoma of the peritoneum during a hernia operation In the remaining 2 cases there was no history of colitis One of the patients had had an abrupt onset with blood stained diarrhoea and operation for acute ileus had in the other revealed a ring carcinoma of the ascending colon subsequent roentgen examination for ascertaining the size of the tumour demonstrated a granular mucosa and small ulcerations in the rectum Advanced annular tumours were found in all 4 cases The patient with involvement of the peritoneum (Fig 11) had a granular mucosa from the rectum to the middle of the descending colon where a 4 cm long stenosis was observed The distinct border of the cuff like stenosis and the ragged and rigid mucosa suggested a malignant neoplasm rather than stenosis due to inflammation, if the stenosis is due to inflammation, the outline is usually smoother and the mucosa of a different pattern BRANCH and SLEDGE however claimed that the differentiation between a neoplasm and an inflammatory lesion could not be made pre operatively and that the presumptive diagnosis in all their 12 instances was carcinoma Our experience is not sufficient to permit any valid conclusions, but we feel *that in such cases* double contrast studies may be useful

It was of course of particular interest to assess the frequency of polypoid tumours in such a colitis series Apart from the 17 cases with pseudopolyposis in which it was not possible to decide with certainty whether a polypoid new formation was present or not we have demonstrated one or more polypoid tumours in 57 (36 5 %) of our 160 cases During the same period we have found one or more polypoid tumours in 1 363 cases (12 %) of our complete



Fig 10 Woman aged 38 Complicating fistulae with abscess



Fig 11 Man aged 28 Granular mucosa and cancer of descending colon

segment of the colon, without small bowel distention, is a sign of impending perforation

Our series also included such a case of dilatation The patient had only slight symptoms at the time of the examination the clinician who had referred the patient for examination believed the disease to be in the healing stage Examination, however, revealed (Fig 9) considerable dilatation of the sigmoid and descending colon and the aboral segment of the transverse colon, while the rectum was narrowed The examination also showed numerous polypous formations, the largest of which were situated in the descending colon

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a



b



c



d

Fig 12 Male aged 17 Symptoms of colitis for 6 months a) Incipient pseudopolyposis with slight shrinkage of caecum and ascending colon as well as ulcerations at hepatic flexure b) About 6 weeks later No symptoms Regression of ulceration progression of pseudopolyposis and shrinkage c) About 5 months after (b) Exacerbation pseudopolyposis and continued shrinkage Recurrent small ulcerations d) About 3 months after (c) Clinical improvement continued shrinkage New ulcerations and alterations of mucosal pattern in descending colon



Fig. 13 Same case as in fig 12 a) About 2 months after the examination illustrated in fig 12d Clinically as before considerable progression in ascending colon complete regression in descending colon b) About 6 months after (a) Clinical progression in spite of cortisone development of fistulae Colectomy performed

material (12 226 patients) The frequency of cases with polypoid tumours was thus at least three times larger in this colitis series a fact which does not permit any conclusions but may nevertheless suggest a certain relation between the two conditions

As mentioned previously it is now possible to follow the course of the disease fairly closely by double contrast studies We have done so in many of our cases and found it useful particularly in the segmental cases where the rectum and sigmoid colon were not involved There is in such cases often a lack of agreement between the patient s symptoms and the course of the disease as judged from the roentgen findings Roentgen changes may often progress despite clinical improvement as exemplified in Figs 12 and 13 The opinion of MOVAT and several others that the roentgen findings at times fail to reflect the severity of the clinical picture whereas the sigmoidoscopic changes closely follow the clinical course is thus by no means without exceptions We feel that a periodic roentgenographic and sigmoidoscopic study of the colon is indicated in all cases of long standing ulcerative colitis since the course is characterized by exacerbations and remissions So called cured cases should also be re examined at regular intervals owing to the risk of malignant degeneration



a



b



c



d

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MOVAT H A Ulcerative colitis Amer J Proctol 7 (1956) 402

PANSDORF H Die Rontgendiagnostik der entzundlichen Dickdarmerkrankungen und ihre Abgrenzung gegenuber dem Carcinom Rontgenpraxis 2 (1930) 732

POPPEL M H and BERANBAUM S L The indenture sign in acute exudative colitis Amer J dig Dis 2 (1957) 382

REIFFERSCHEID M Das Spatschicksal des Colitis ulcerosa Kranken Arch klin Chir 293 (1960) 558

RICKETTS W E KIRSNER J B and PALMER W L Chronic non specific ulcerative colitis Gastroenterology 10 (1948) 1

RIPSTEIN C B Perforation of colon in ulcerative colitis Ann Surg 140 (1954) 872

ROSENQVIST H LAGERCRANTZ R ÖHRLING H and EDLING N Ulcerative colitis and carcinoma coli Lancet I (1959) 906

SLANEY G and BROOKE B N Cancer in ulcerative colitis Lancet (1959 II) 694

SPRATT J S ACKERMAN L V and MOYER C A Relationship of polyps of the colon to colonic cancer Ann Surg 148 (1958) 682

STEVENSON C A and WILSON M Indications for the double contrast colon examination Amer J Roentgenol 71 (1954) 398

STIERLIN E Die Radiographie in der Diagnostik der Ileozoekaltuberkulose und anderer Krankheiten des Dickdarms Munch med Wschr 58 (1911) 1231

WELIN S Modern trends in diagnostic roentgenology of the colon Brit J Radiol 31 (1958) 453

SUMMARY

A material of 160 cases of ulcerative colitis examined by a modification of the double contrast method is reported This means of investigation has proved more effective than the usual barium enema The diagnosis of the condition is considered and the common complication of malignant degeneration discussed

ZUSAMMENFASSUNG

Ein Material von 160 Fallen mit ulzeroser Colitis wird vorgelegt welches mit Hilfe einer Modifikation der Doppelkontrastmethode untersucht worden ist Diese Untersuchungstechnik hat sich effektiver als der ubliche Bariumeinlauf erwiesen Die Diagnose der Erkrankung wird erwahnt und die gewohnliche Komplikation der malignen Degenerierung wird besprochen

RÉSUMÉ

Presentation d une série de 160 cas de colite ulcéreuse examines par une modification de la méthode de double contraste Cette technique d examen s est montrée supérieure au lavement baryté habituel Les auteurs étudient le diagnostic de cette affection et examinent sa complication fréquente par dégénérescence maligne

REFERENCES

ANDRÉN L and WELIN S Über die Haufigkeit von Kolonpolypen bei ulzeroser Kolitis Fortschr Rontgenstr 92 (1960) 567
BACON H E Ulcerative colitis J B Lippincott Philadelphia 1958
BARGEN J A and COMFORT M W Association of chronic ulcerative colitis and multiple polyps Ann intern Med 4 (1930) 122
BRANCH B D and SLEDGE C B Inflammatory lesions of the colon simulating neoplasms Gastroenterology 28 (1955) 981
BUCKSTEIN J The digestive tract in roentgenology Vol II 2nd ed J B Lippincott Philadelphia 1953
CATTELL, R B Surgical treatment of ulcerative colitis Gastroenterology 10 (1948) 63
COUNSELL P B and DUKES C E The association of chronic ulcerative colitis and carcinoma of the rectum and colon Brit J Surg 39 (1952) 485
DICK A C BERRIDGE F R and GRAYSON M J The pathological basis of the radiological changes in ulcerative colitis A study of cases treated by colectomy Brit J Radiol 32 (1959) 432
FELDMAN M Clinical roentgenology of the digestive tract 4th ed William & Wilkins Baltimore 1957
FELSEN J and WOLARSKY W Chronic ulcerative colitis and carcinoma Arch int Med 84 (1949) 293
HAWKES, S Z and SHIELDS R K Adenomatosis versus pseudopolyposis of large bowel Bull U S Army med Dep 6 (1946) 302
JOHNSON T M and ORR T G Carcinoma of colon secondary to chronic ulcerative colitis Amer J dig Dis 15 (1948) 21
KALIL T H and ROBBINS L L Early roentgenologic changes in idiopathic ulcerative colitis Radiology 53 (1949) 1
LUMB, G PROTHEROE R H B and RAMSAY G S Ulcerative colitis with dilatation of the colon Brit J Surg 43 (1955) 182

MONAT H A Ulcerative colitis Amer J Proctol 7 (1956) 402
PANSDORF H Die Röntgendiagnostik der entzündlichen Dickdarmerkrankungen und ihre Abgrenzung gegenüber dem Carcinom Röntgenpraxis 2 (1930) 732
POPPEL, M H and PERANSBAUM S L The indenture sign in acute exudative colitis Amer J dig Dis 2 (1957) 382
REIFFERSCHEID M Das Spätschicksal des Colitis ulcerosa Kranken Arch klin Chir 293 (1960) 558
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Fig 1 Ca diac catheter in the left main pulmonary artery with the streamer n the main branch supplying the lower lobe (Sl ght left anter or oblique position)



a b

F g 2 The t p of the catheter i in the outflow tract of the right ventricle During systole the st eamer s carried toward the or fice of the pulmonary artery In diastole it falls back mo e m dially

FROM THE DEPARTMENT OF RADIOLOGY, YALE UNIVERSITY MEDICAL SCHOOL, NEW HAVEN, U S A

DEMONSTRATION OF BLOOD CURRENTS WITH RADIOPAQUE STREAMERS

by

T DOBY and R M LOWMAN

As long as 450 years ago Leonardo da Vinci tried to see streamlines in his glass model of the heart No one attempted to re check his experiments until recent advances in radiology permitted us to show the flow and whirling of the blood in the heart chambers themselves

Some years ago when the finer details of angiocardiography were investigated more extensively, blood currents began to be demonstrated The opaque jet through pulmonary valvular stenosis, ventricular septal defect and patent ductus arteriosus were recognized Non opaque jets shooting into already opacified compartments were also noted The usual disadvantages encountered were the dimness of the jet outline and its rapid disappearance in the course of the angiographic procedure A single film, or a few of the series only, showed the jet satisfactorily

In vitro, or animal experiments, genuine, or radiopaque oil droplets can be followed (McDONALD et coll , DOTTER et coll and STRAUFFER), by which the speed and direction of the currents may be demonstrated, but the observation is limited by the fairly rapid disappearance of the droplets from the area of study The embolizing effect of the oil makes this kind of procedure impossible for humans

The idea of observing blood currents by the use of radiopaque dots attached to easily movable threads at the end of cardiac catheters, was suggested from the observation of windblown banners, or ribbons, at the top of masts of

This work was supported by a U S Public Health Service Grant No H-4834 (Rad)
Submitted for publication 21 November 1960

and moved individually Most of the time single threads were used When the catheters were pushed as far as the main pulmonary artery, the blood current carried the streamers into secondary divisions, without allowing flapping in the narrow lumen of the artery

When the catheters were pulled back the streamers entered the ventricle and later the atrium where with more room they flapped around in the currents Under the image amplifier they showed considerable whirling and were moved easily in all directions No blood clots could be found at the dots after withdrawal of the catheters Technical details of the preparation and handling of the radiopaque dots and catheters are published elsewhere (DOBY)

Whether the described principle can be utilized to diagnose shunts or back jets opposite normal flow through insufficient valves in human subjects, will be decided by further examinations

Acknowledgement

We wish to thank Dr H J Ricketts for his technical help and practical suggestions as surgeon in our experiments

SUMMARY

Radiopaque streamers show the blood currents in cardiac chambers The excursions caused by the flow of blood can be watched for a long time without danger to the experimental animal Practical implications are suggested

ZUSAMMENFASSUNG

Rontgendichte Wimpel zeigen den Blutumlauf in den Herzkammer Die durch den Blutstrom erzeugten Exkursionen konnen langere Zeit ohne Gefahr fur das Versuchstier beobachtet werden Praktische Anwendungsmoglichkeiten werden hervorgehoben

RÉSUMÉ

Des banderoles radio opaques mettent en évidence les *courants sanguins* dans les cavités cardiaques On peut observer longuement sans danger pour l animal d expérience leurs mouvements dus à l écoulement du sang *Les auteurs examinent* les conséquences pratiques de ces expériences

REFERENCES

DA VINCI LEONARDO Quaderni d anatomia I—VI C L Vangensten A Fonahn & H Hopstock, Christiania 1911—1916

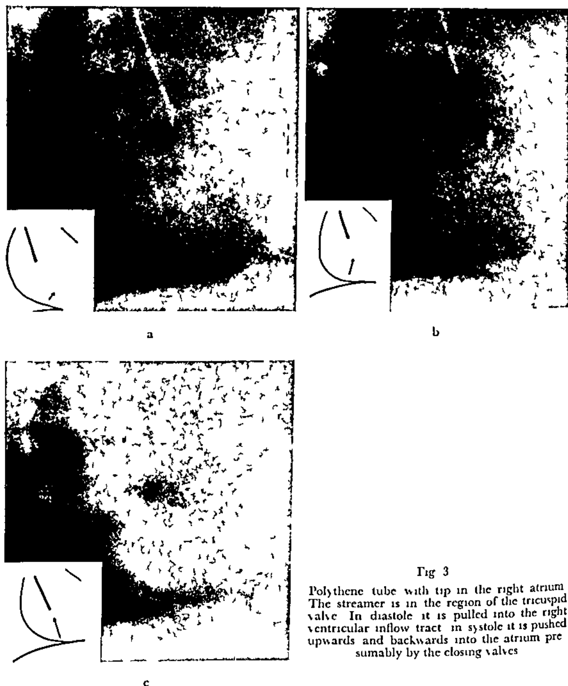
DOBY T Preparation of radiopaque streamers to show blood currents in heart chambers (In press)

DOTTER C T and FRISCHE L H Radiologic technique for qualitative and quantitative study of blood flow Circulation 18 (1958) 961

MCDONALD D A and POTTER J M Flow patterns in arteries recorded by high speed cinematography J Phys 109 (1949) 17 P

POTTER J M and MCDONALD D A Cinematographic recording of the velocity of arterial blood flow Nature 166 (1950) 596

STAUFFER, H Lipiodol droplets followed in the blood vessels of experimental animals Private communication 1960



a

b

c

Fig 3

Polythene tube with tip in the right atrium The streamer is in the region of the tricuspid valve In diastole it is pulled into the right ventricular inflow tract in systole it is pushed upwards and backwards into the atrium presumably by the closing valves

yachts in a race The catheters prepared for this purpose were led into the right ventricles of dogs The procedure was filmed under fluoroscopic control with a 16 mm cine unit at 30 frames/sec through a 7 1/4″ Picker image amplifier

Several kinds of radiopaque streamers were used Those containing up to seven individual nylon threads with a radiopaque dot at one end of each tended to entangle in blood clots Those containing only two threads kept apart



Abb 1 a) Am Schlu s der Injekt on von 20 ml Triopac 300 F nen Teil des Kontrastmittels ist im Kapillarnetz d Leber orhanden b) Zwei Minuten spater E n betrachtlicher Te l des Kontrast m ttel hat das M lz Pfortader System schon verlassen doch sind immer noch ein ge der kleinen Pfo tad raste p all g fullt

so dass die Darstellung des Lebers erleichtert wird Etwa 20 Minuten nach der Morphininjektion versetzte man die Hunde in tiefe Athernarkose die wahrend der ganzen Versuchsdauer unterhalten wurde

Ein zweikanaliger Katheter ,Rusch Super Nr 12 wurde in V femoralis und durch der V iliaca und der V cava inferior bis zur Hohe der Zwerchfell gewolbe eingefuhrt Wegen der Unmoglichkeit die Milz beim Hunde per kutan zu punktieren erreichte man sie durch Laparotomie Mit einer Nadel von 0 8 mm Lumen in das Milzparenchym wurde ein hochkonzentriertes wasserlosliches Kontrastmittel (70 %ige Losung von Diodon Triopac 300 Triopac 400) in einer Menge von 1 ml/kg Korpergewicht eingefuhrt Nach Einfuhrung der Halfte des Kontrastmittels (etwa 2 Sekunden nach Injektions beginn) fullte man durch den einen Katheterkanal den Gummiballon des Katheters gleichfalls mit Kontrastmittel wodurch in den Lebervenen eine Stauung ausgelost wurde Das Kontrastmittel bleibt im Kapillarnetz der Leber gestaut und macht so alle ihre Abschnitte sichtbar

Technik Vor der Injektion des Kontrastmittels wird eine Ubersichtsauf nahme der oberen Bauchhalfte gemacht Am Schluss der Injektion macht

AUS DER ABTEILUNG FÜR RÖNTGENOLOGIE UND RADIOLOGIE (DIREKTOR PROF. G. TENTSCHOV), DES INSTITUTS FÜR ÄRZTLICHE FACHSCHULUNG UND FORTBILDUNG, SOFIA, BULGARIEN

HEPATOGRAPHIE MIT WASSERLÖSLICHEN KONTRAST-MITTELN IM TIERVERSUCH

von

G. Gospodinow und L. Welitschkow

Die Erkennung zystischer, primärer und metastatischer Neubildungen der Leber bereitet immer noch erhebliche Schwierigkeiten, wiewohl in den letzten Jahren einige neue Verfahren, darunter auch die lienoportale Venographie, eingeführt wurden.

Die vorliegende Mitteilung ist das Ergebnis unserer experimentellen Untersuchungen an 6 Hunden, wo wir versucht haben die Leber besser darzustellen und zu explorieren. Im Hinblick darauf, dass die Passage des Kontrastmittels bei der gewöhnlichen lienoportalen Venographie ziemlich schnell vor sich geht und also die Anfärbung des Lebers bei der Passage des Kontrastmittels durch das Kapillarnetz nur unbedeutlich dichter hervortritt, zielten wir in unseren Versuchen darauf ab, auf kurze Zeit die Passage des Kontrastmittels in der Kapillarphase aufzuhalten. Das liess sich durch eine auf mechanischem Wege erzeugte Stauung in den Lebervenen erreichen, und zwar durch Blockierung der unteren Hohlvene oberhalb der Einmündungsstelle der Lebervenen.

Methode. Für die Versuche dienten Hunde von 14 bis 20 kg Körpergewicht. Als Vorbereitung erhielten die Hunde 0,02 g Morphin je Kilogramm Körpergewicht, wodurch sie beruhigt werden und überdies (infolge des ausgelösten Erbrechens und der Defäkation) der Magen- und Darminhalt entleert wird,

Bei der Redaktion am 29. August 1960 eingegangen.



Abb. 1. a) Am Schluss der *Injektion von 20 ml Triopac 300*. Einen Teil des Kontrastmittels ist im Kapillarnetz der Leber vorhanden. b) Zwei Minuten später. Ein beträchtlicher Teil des Kontrastmittels hat das Milz-Pfortader-System schon verlassen, doch sind immer noch einige der kleinen Pfortaderäste prall gefüllt

so dass die Darstellung des Lebers erleichtert wird. Etwa 20 Minuten nach der Morphininjektion *versetzte man die Hunde in tiefe Äthernarkose*, die während der ganzen Versuchsdauer unterhalten wurde.

Ein zweikanaliger Katheter Rusch Super Nr. 12 wurde in V. femoralis und durch der V. iliaca und der V. cava inferior bis zur Höhe der Zwerchfellgewölbe eingeführt. Wegen der Unmöglichkeit, die Milz beim Hunde perkutan zu punktieren, erreichte man sie durch Laparotomie. Mit einer Nadel *von 0.8 mm Lumen in das Milzparenchym wurde ein hochkonzentriertes* wasserlösliches Kontrastmittel (70 %ige Lösung von Diodon, Triopac 300, Triopac 400) in einer Menge von 1 ml/kg Körpergewicht eingeführt. Nach Einführung der Hälfte des Kontrastmittels (etwa 2 Sekunden nach Injektionsbeginn) füllte man durch den einen Katheterkanal den Gummiballon des Katheters gleichfalls mit Kontrastmittel, wodurch in den Lebervenen eine Stauung ausgelöst wurde. Das Kontrastmittel bleibt im Kapillarnetz der Leber gestaut und macht so alle ihre Abschnitte sichtbar.

Technik. Vor der Injektion des Kontrastmittels wird eine Übersichtsaufnahme der oberen Bauchhälfte gemacht. Am Schluss der Injektion macht



Abb. 2. Aufnahme in der 6. Minute vom Injektionsschluss linker Seitenlage. Die Grenzen der ganzen Leber und einiger der Leberteile sind klar umrissen.

man eine Aufnahme in Rückenlage. Darauf sieht man sehr gut gefüllt V. lienalis, die V. portae und deren Verästelungen. Einen Teil des Kontrastmittels erblickt man auch im Kapillarnetz der Leber (Abb. 1a). Zwei Minuten nach der Injektion hat man eine starke Kontrastmittelspeicherung der Leber (Abb. 1b). Man sieht, dass ein beträchtlicher Teil des Kontrastmittels das Milz-Pfortader-System schon verlassen hat, doch sind immer noch einige der kleinen Pfortaderäste prall gefüllt. In der 4. bzw. 6. Minute vom Injektionsschluss macht man Aufnahmen in rechter bzw. linker Seitenlage. Darauf sieht man die Grenzen der ganzen Leber und auch einiger der Leberteile klar umrissen (Abb. 2). In einigen Fällen wurde Tomographie versucht — 4 Schnitte über je 2 cm auf der Höhe der Leber. Auf solchen Bildern treten die Lebergrenzen deutlich hervor. Die Stauung in den Lebervenen hielt etwa 6 Minuten an und wurde nach der letzten Aufnahme behoben. Während der Untersuchung spritzte man einigemal eine Lösung zitronensauren Natriums durch den einen der Katheterkanäle zwecks Vorbeugung von Gerinnselbildung ein.

Um das Verfahren auf seine Harmlosigkeit zu prüfen, tötete man die Hunde mit schwefelsaurem Magnesium (intrakardial) in verschiedenen Abständen vom Tage der Untersuchung, zwischen dem 3. und 45. Tage. Ausser der makroskopischen Untersuchung der Milz, Leber, der Nieren, der unteren Hohlvene, der Pfortader und der V. lienalis, machte man auch eine

histologische Untersuchung verschiedener Abschnitte derselben (Dr Dost schinov), ohne irgendwelche Befunde einer Schadigung

Man wahlte den Einführungsweg des Kontrastmittels durch eine Milz punktion im Hinblick auf die Moglichkeit bei einer Anwendung des Verfahrens am Menschen, die Milz perkutan zu punktieren

ZUSAMMENFASSUNG

Eine Methode fur Hepatographie wird beschrieben die eine betrachtliche Verbesserung der Abbildung des Milz Pfortader Systems erzielt Durch Verzogerung der Kontrastmittel passage wird die Leber sehr deutlich sichtbar und die Kontrastmittelspeicherung ist intensiv genug um Kontrastdefekte auseinanderzuhalten, deren Substrat zystische primarneoplastische oder metastatische Neubildungen sind

SUMMARY

A method of hepatography which produces considerable improvement in the demonstration of the lienoportal system is described The slowness of the passage of the contrast medium ensures good filling of the liver and the degree of opacity obtained is such that contrast defects due to cysts primary growths or metastatic deposits may be differentiated

RESUMÉ

Les auteurs decrivent une methode d hépatographie qui améliore considérablement la mise en evidence du systeme spleno-portal La lenteur du passage du moyen de contraste assure une bonne imprégnation hepatique et le degré d opacite obtenu est tel qu il permet de distinguer les defauts de contraste dus a des kystes à des tumeurs primitives ou a des metastases

SCHRIFTTUM

Abeatici S et Campi L Sur les possibilités de l angiographie hepatique La visualisation du systeme portal Acta radiol 36 (1951) 383

Child Ch O Sullivan W Payne M and McClure R Portal venography Radiology 57 (1951) 691

Csakany G und Tardos Z Splenoporto-Hepatographie Tierversuche Fortschr Ront genstr 92 (1960) 410

Moore G and Bridenbaugh R Roentgen demonstration of the venous circulation in the liver portal venography Radiology 57 (1951) 685

Rappaport A M Hepatic venography Acta radiol 36 (1951) 165

Rigler L Olfeld I and Krumbach R Roentgen hepatography by injection of a contrast medium into the aorta Radiology 60 (1953) 363

Shishkin V I Splenoportographia (In Russian) Vestn Rentgenol Radiol 5 (1955) 79

— Krakowski N I und Zodiev V V Über die Methodik der Splenoportographie und ihre diagnostische Bedeutung Vestn Rentgenol Radiol. 21 (1956) 54 (r)

Stattin Sture Percutaneous lieno-portal venography in the demonstration of liver masses Acta radiol 52 (1959) 353

Thomas Sidney F Henry George W and Kaplan Henry S Hepatolienography Past present and future Radiology 57 (1951) 669

Tori G Hepatic venography in man Acta radiol 39 (1953) 89



Abb 2 Aufnahme in der 6 Minute vom Injektions schluss linker Seitenlage Die Grenzen der ganzen Leber und einiger der Leberteile sind klar umrissen

man eine Aufnahme in Ruckenlage Darauf sieht man sehr gut gefullt V lienalis, die V portae und deren Verastelungen Einen Teil des Kontrast mittels erblickt man auch im Kapillarnetz der Leber (Abb 1a) Zwei Minu ten nach der Injektion hat man eine starke Kontrastmittelspeicherung der Leber (Abb 1b) Man sieht dass ein betrachtlicher Teil des Kontrastmittels das Milz Pfortader-System schon verlassen hat, doch sind immer noch einige der kleinen Pfortaderaste prall gefullt In der 4 bzw 6 Minute vom Injek tionsschluss macht man Aufnahmen in rechter bzw linker Seitenlage Darauf sieht man die Grenzen der ganzen Leber und auch einiger der Leberteile klar umrissen (Abb 2) In einigen Fallen wurde Tomographie versucht — 4 Schnitte uber je 2 cm auf der Hohe der Leber Auf solchen Bildern treten die Lebergrenzen deutlich hervor Die Stauung in den Lebervenen hielt etwa 6 Minuten an und wurde nach der letzten Aufnahme behoben Wahrend der Untersuchung spritzte man einigemal eine Losung zitronensauren Natriums durch den einen der Katheterkanale zwecks Vorbeugung von Gerinnsel bildung ein

Um das Verfahren auf seine Harmlosigkeit zu prufen totete man die Hunde mit schwefelsaurem Magnesium (intrakardial) in verschiedenen Abstanden vom Tage der Untersuchung, zwischen dem 3 und 15 Tage Ausser der makroskopischen Untersuchung der Milz, Leber, der Nieren, der unteren Hohlvene, der Pfortader und der V lienalis, machte man auch eine

WANNAGAT L Bedeutet die laparoskopische Splenoportographie einen Fortschritt auf dem Gebiete der medizinischen Röntgendiagnostik? Fortschr Röntgenstr 84 (1956) 509

ZEGER Z ALBOT G et ARVAY, N La phlébographie portale dans l exploration des affections hépatospléniques Presse méd 59 (1951) 1230

ZODIEV V V SILAGIN P V und LASTATNEEVA W Das Verfahren der Portovenographie und seine diagnostische Bedeutung Vestn Rentgenol Radiol 2 (1955), 58

FROM THE RADIOISOTOPE RESEARCH LABORATORY (DIRECTOR PROF G NYLIN) AND THE HEART CLINIC (DIRECTOR DOCENT S AKESSON) SODERSJUKHUSET, STOCKHOLM, SWEDEN

CEREBRAL CIRCULATION STUDIED WITH LABELLED RED CELLS IN HEALTHY MALES

by

GUSTAV NYLIN SVEN HEDLUND and OLOF REGNSTROM

Serial angiography has been used for the determination of the cerebral circulation time The results obtained depend on the technique employed and have sometimes varied considerably (MONIZ 1932, SCHURR & WICKBOM 1952 GREITZ 1956 TONNIS & SCHIEFER 1959 and others) It has been shown that the speed of the cerebral circulation differs in the arterial and venous phases and that marked changes occur in pathologic cases

The *cerebral blood flow* has been studied previously by NYLIN et coll (1955 1958 and 1960) and some recent work is *in the press* In the present paper some further information on the results obtained in studies of the cerebral blood flow blood volume and circulation time in healthy males is given and the dilution curves forming the basis of the calculations are presented in a series of diagrams

Material and Method Thirty four healthy males all volunteers aged between 26 and 53 years (mean 36 years) were studied They were carefully examined prior to the circulatory studies the histories state of the general and neurologic systems as well as the heart volume determinations and ECG being all recorded No abnormality was found

Following an injection of a small dose of morphine scopolamine the subject was placed in the recumbent position The two internal jugular bulbs and the internal carotid arteries

Submitted for publication 10 November 1960

may depend partly upon the anatomy of the cerebral veins, but also upon the flow being laminar in the sagittal sinus which we presume prevents the complete mixing of the blood from the two hemispheres This opinion is supported by the investigations of HELPS and McDONALD (1954) and NYLIN et coll (1960)

The dilution curves obtained for the two bulbs are as a rule identical after the intravenous injection when all arteries to the brain are provided with labelled red cells In 8 cases or 28 % of the present material slightly asymmetrical curves from the two bulbs were obtained, in only one case (Fig 9) was the asymmetry marked In clinical cases, such as those of cerebral atherosclerosis nonsymmetrical curves are mostly found this will be dealt with in another paper

The values of the cerebral blood flow varied from 667 ml to 1 238 ml, with a mean of 915 ml in the present material, the mean is 11 9 per cent of the cardiac output which was determined as averaging 7 900 ml No correlation was observed between the cardiac output and the cerebral blood flow nor was any correlation found between the cerebral blood flow and the age of the subjects in the present series

The cerebral blood volume varied from 87 ml to 183 ml, with a mean of 132 ml this being 2 7 per cent of the total blood volume of the body The mean of the total blood volume was 5 230 ml

The circulation times based on the dilution curves from the two internal jugular veins after the injections into both the carotid arteries are shown in the Table on next page There were only slight variations in the determined values The appearance time and peak concentration times were shorter from the ipsilateral bulb than from the contralateral bulb but the values for the disappearance time were about the same For the parameters mentioned, the same values were found for both the ipsilateral and the contralateral bulb irrespective of whether the labelled cells were injected into the right or the left carotid artery The appearance time varied in general from 2 to 4 sec for the ipsilateral and from 3 to 5 sec for the contralateral bulb the peak concentration time varying from 5 to 7 sec for the ipsilateral and from 6 to 8 sec for the contralateral bulb The disappearance time was generally from 12 to 16 sec for both bulbs There were only two exceptions for rather high values (*Figs 6 and 12*) No correlation was found to exist between these parameters of circulation time and age In our material of old people up to 80 years of age we have observed perfectly normal and short circulation times for example in a 77 year old woman with slight hypertension (*Fig 2*)

The mean circulation time calculated from the intravenous injection was found to be 8 5 sec with an average range of from 7 to 10 sec There was no correlation between the mean circulation time and the cerebral blood flow in the present series of normal males

were punctured percutaneously and a first intravenous injection of 1 5 ml of the subjects own labelled blood, with simultaneous sampling at one second intervals from the two jugular bulbs and one carotid artery, were performed Injections of the same amount of blood into two carotid arteries one after the other were then made and samples from the bulbs were withdrawn after each injection The techniques used have been previously described (NYLIN et coll 1958 1960)

The blood pressure and pulse rate were continuously recorded before and during the examination It was noted that these were within the limits of the normal values under basal conditions No obvious discomfort or complications were observed in any of the cases examined

The calculation of the cerebral blood flow was based on the four dilution curves obtained from the jugular bulbs after the two injections into the internal carotid arteries The mathematical derivation of the equations has been given in a paper by ANDERSSON (1957) and NYLIN et coll (1960) It is important that the injections be performed sufficiently high up in the internal carotid artery to avoid regurgitation into the external carotid artery In a few cases, however slight regurgitation cannot be excluded with certainty and may have caused an error in the calculation of the cerebral blood flow If the sum of the activity of the two ipsilateral peaks in pro mille of injected activity is high or above 30 to 40 it is very probable that most or all the activity has reached the brain, as indicated in our earlier publications The product of the cerebral blood flow and the mean circulation time represents the cerebral blood volume The mean circulation time has been calculated from the results obtained during the intravenous injection

The circulation times through the brain were determined from the dilution curves obtained from the jugular bulbs after the two carotid injections The values are represented by the appearance time (App) the peak concentration time (Peak) and the disappearance time (Disapp) for ipsilateral and contralateral dilution curves The disappearance time is defined as the time when the down slope of the curve reaches a constant level

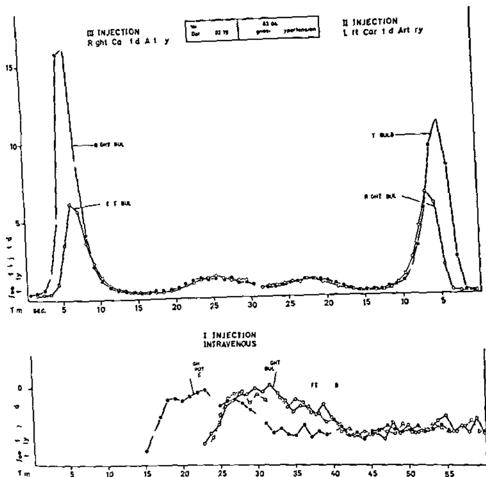
Results

The dilution curves obtained are recorded in Figs 1 to 25 Some of the studies are incomplete due to difficulties in puncturing both the internal carotid arteries on the same occasion The age of the subjects may be found from data recorded in the diagrams

The contralateral bulb generally drains less activity than the ipsilateral one, as shown in the figures Not infrequently however, the injected erythrocytes are drained symmetrically through the two bulbs after one carotid injection This occurred in 10 cases in the present material, in 8 cases either no or only very slight activity was drained from the contralateral bulb after one intracarotid injection and in 2 cases the injection was made into the external carotid artery and no activity at all passed via the brain into the jugular bulbs (Figs 15 and 23)

When the flow through the right and the left jugular bulb is calculated separately, the right bulb drains more of the cerebral blood flow than the left bulb, i e on an average 62 % of the cerebral blood flow passes through the right bulb and 38 % through the left bulb

The asymmetrical drainage of the labelled cells through the jugular bulbs



F g 2

/7 years

Right car art	Ip ilat bulb	Contralat bulb	Left car art	Ipsilat. bulb	Contralat bulb
App	4 sec	5 sec	App	3 sec	4 sec
P ak	6	7	Peak	5 »	7 »
Disapp	13	13 »	Disapp	13 »	13 »

C rd ac output 6 500 ml/m n
Mean c culation t m 9 1 sec

Total blood volume 4 191 ml
Heart volume 6/0 ml 410 ml/m

Table

The cerebral circulation times in seconds in healthy males (from carotid artery to jugular bulb)

		App	Peak	Disapp
Injection into right carotid artery				
Ipsilateral bulb	(mean value)	3.2	6.2	14.2
	(number of cases)	(27)	(27)	(27)
	(range)	2—5	4—10	12—20
Contralateral bulb	(mean value)	4.5	7.1	13.1
	(number of cases)	(24)	(24)	(24)
	(range)	3—6	6—9	9—18
Injection into left carotid artery				
Ipsilateral bulb	(mean value)	3.1	6.1	14.9
	(number of cases)	(24)	(24)	(24)
	(range)	2—4	4—8	12—21
Contralateral bulb	(mean value)	4.0	6.7	13.9
	(number of cases)	(25)	(25)	(25)
	(range)	2—6	5—8	11—16

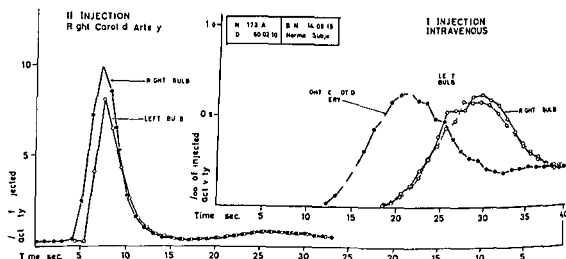


Fig 1

46 years

Right car art	Ipsilat bulb	Contralat bulb
App	5 sec	6 sec
Peak	7 »	7 »
Disapp	14 »	14 »

Cardiac output 7 000 ml/min
Mean circulation time 7.8 sec
Total blood volume 5 598 ml
Heart volume 810 ml 360 ml/m²

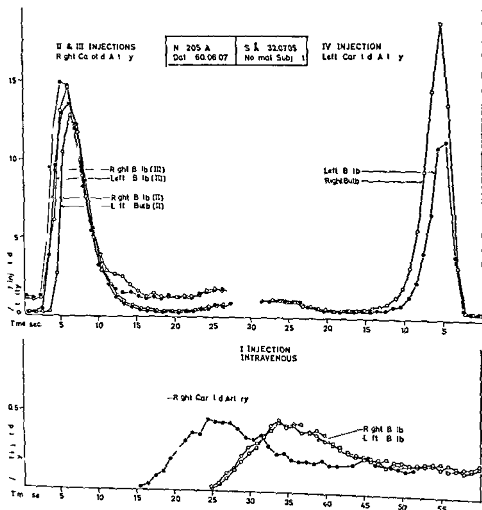


Fig 4

28 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat. bulb
App	3 sec	ɔ sec	App	3 sec	3 sec
Peak	6 »	7 »	Peak	5 »	5 »
Disapp	15	15 »	Disapp	13 »	12 »

Cer b al blood flow 943 ml/min (12 5 of cardiac output)
Cer b al pool volume 155 ml (2 6 of total blood volume)
Ca d ac output 7 500 ml/min
Total blood volume 6 045 ml

Mean c culation t me 9 9 sec
Heart volume 670 ml 350 ml/m

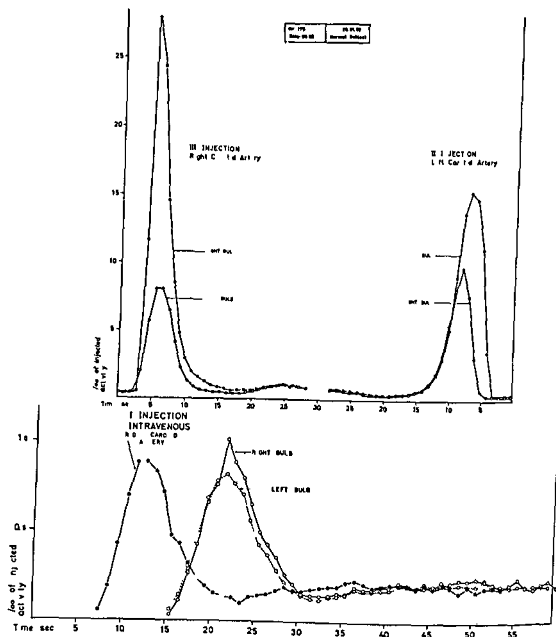


Fig 3

35 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	3 sec	App	4 sec	5 sec
Peak	5 »	6 »	Peak	7 »	8 »
Disapp	15 »	13 »	Disapp	15 »	15 »

Cerebral blood flow 824 ml/min (10 2 % of cardiac output)
Cerebral pool volume 130 ml (2 4 % of total blood volume)
Cardiac output 8 100 ml/min
Mean circulation time 9 5 sec

Total blood volume 5 334 ml
Heart volume 720 ml 380 ml/m²

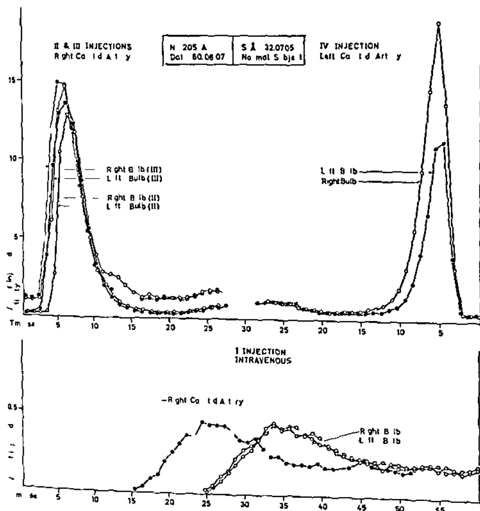


Fig 4

78 years

Right car art	Ip ilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	3 sec	App	3 sec	3 sec
Peak	6 »	7 »	Peak	5 »	5 »
Disapp	15 »	15 »	Disapp	13 »	12 »

Cerebral blood flow 943 ml/min (12 5 of ca diac output)
Cerebral pool v l m 155 ml (2 6 of total blood volume)
Card c o tput 7 00 ml/min
Total blood volume 6 045 ml

Mean circulation time 9 9 sec
Heart volume 670 ml 350 ml/m

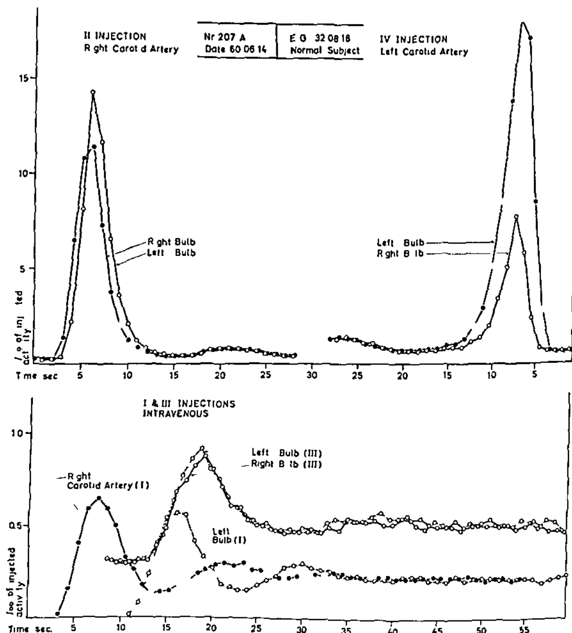


Fig. 5 — 28 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	4 sec	App	3 sec	4 sec
Peak	6 »	6 »	Peak	7 »	7 »
Disapp	13 »	14 »	Disapp	16 »	14 »

Cerebral blood flow 1 219 ml/min — Cerebral pool volume 159 ml (3 3 % of total blood volume)
Mean circulation time 7 8 sec — Total blood volume 4 859 ml — Heart volume 640 ml 360 ml/m

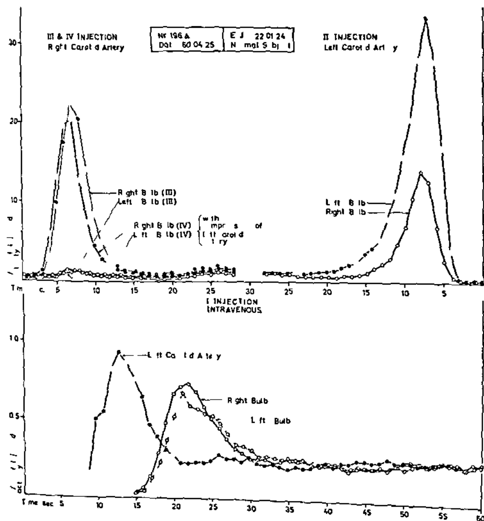


Fig 6

8 years

R ght ar art	Ip slat bulb	Contralat bulb	Left car art	Ips lat bulb	Contralat bulb
App	3 sec	5 sec	App	4 sec	5 sec
I ak	6 »	7 »	Peak	7 »	8 »
Disapp	13 »	10 »	Disapp	18	15 »

Cereb al blood flow 6(7 ml/m n (8 8 of cardiac output)
C rebral pool volume 116 ml (2 8 of total blood volume)
Card c output 7 (00 ml min
Mean c culation time 10 4 sec

Total blood volume 4 151 ml
Heart volume 610 nl 337 ml m

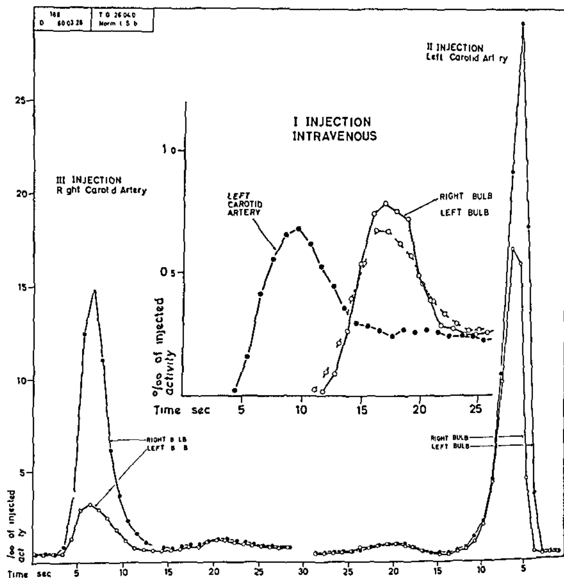


Fig 7

34 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	4 sec	App	3 sec	4 sec
Peak	6 »	6 »	Peak	6 »	7 »
Disapp	13 »	12 ›	Disapp	13 »	13 »

Cerebral blood flow 1 077 ml/min (11 4 % of cardiac output)
Cerebral pool volume 126 ml (2 9 % of total blood volume)
Cardiac output 9 400 ml/min
Total blood volume 4 320 ml

Mean circulation time 7 0 sec
Heart volume 600 ml 340 ml/m²

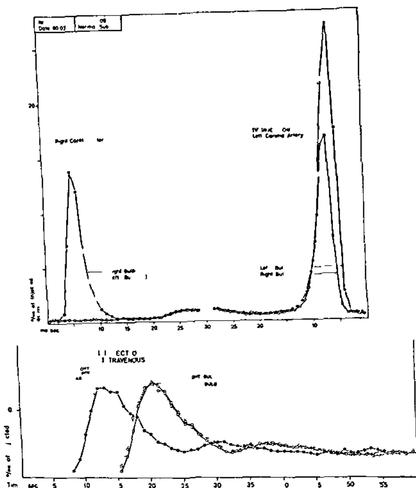


Fig 8 — 32 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	0 sec	App	4 sec	5 sec
Peak	5 »	0 »	Peak	6 »	6 »
Disapp	12	0 »	Disapp	14 »	14 »

Cer b al blood flow 948 ml m n (1? ɔ of ca diac output)
Ce bral poo l 1 m 120 ml (? 1 of total blood olume)
Cardia utput 7 600 ml m n
M an c culation t me 7 6 sec

Total blood volume ɔ 6?1 ml
Heart volume /80 ml 420 ml/m

Nr 204 B
Date 60 06 01
R N. 29 12 29
Normal Subject

II & III INJECTIONS
L ft Carot d A tery

L ft B lb (III)
R ght Bulb (III)
Left Bulb (II)
R ght Bulb (II)

I INJECTION
INTRAVENOUS

Left Carotid Artery

Right Bulb
L ft B lb

Time sec.

Fig 9 31 years

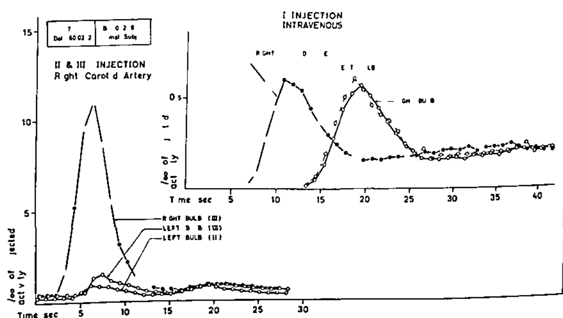


Fig 10 30 years

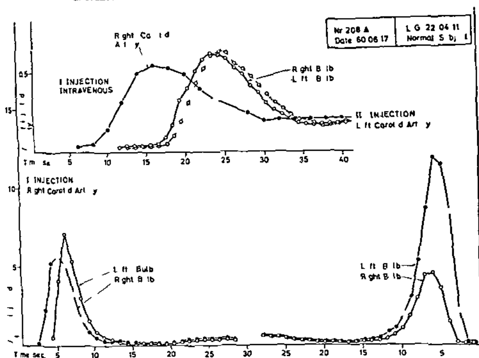


Fig 11 38 years

Right car art	Ips lat bulb	Contralat bulb	Left car art	Ip ilat bulb	Contralat bulb
App	3 sec	4 sec	App	2 sec	3 sec
P k	6	7	Peak	6 »	6 »
D sapp	12	14	Disapp	15 »	14 »

Cardiac output 7 100 ml m n
T tal blood volume 8 716 ml

Mean c c lat on time 6 1 sec
Heart volume 800 ml 410 ml/m

Legend for F g 9 (oppos e page)

Left ca art	Ip lat bulb	Contralat bulb
App	3 sec	4 s
P ak	6	6
Disapp	1C	13

Cer b al blood fl 1 238 n l m n (1) 2 of card ac output)
Ce ebral pool ol m 16 ml (3 2 of total blood vol me)
Ca d a output 8 700 ml m n
M an cul t on t me 8 0 sec

Total blood volume 5 233 ml
Heart olume 620 ml 320 ml/m

Leg nd for Fig 10 (oppo te page)

R ght car a t	Ips l t l ulb	Cont alat bulb
App	3 sec	5 sec
Peak	6 »	7
Disapp	13	1

Card ac output 11 00 ml min
Mean circulation t me 7 6 sec
Total blood olume 5 394 ml
Heart olume 7 0 ml 400 ml m

Nr 193 A
Date 60 04 11
J K P 28 07 08
Normal Subject

II INJECTION
R ght Carot d Artery

III INJECTION
Left Carot d Artery

I INJECTION
INTRAVENOUS

0.5

°/oo of injected activity

Time sec 15 20 25 30 35

R ght Bulb
Left Bulb

Left Bulb
R ght B lb

25 20 15 10 5

°/oo of injected act ity

Time s c. 5 10 15 20 25 30 25 20 15 10 5

Fig 12

3? years

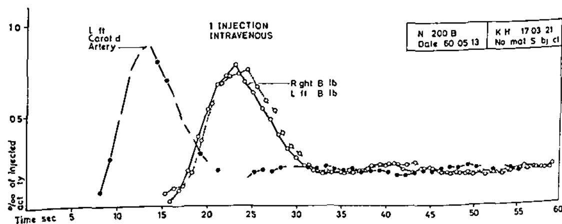
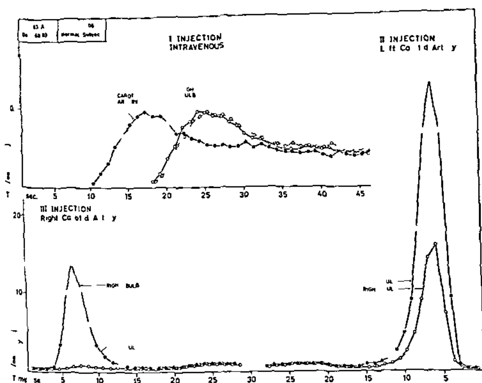


Fig 13

43 years



F g 14 46 years

R ght car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	4 sec	6 sec	App	3 sec	4 sec
P ak	7 »	8	Peak	6 ›	6
Disapp	14 »	1? ›	Disapp	16 ›	16 »

Ce ebral blood flow 1 115 ml/min (15 1 of cardiac output)
Cereb al pool olume 167 ml (3 ? of total blood volum)
Cardiac output 7 400 ml/min Total blood olume 5 197 ml
Mean c rculation time 9 0 sec Heart olume 8?0 ml 3?0 ml m

Legend for Fig 12 (opposite page)

R ght car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	5 sec	App	3 sec	4 sec
P ak	7 »	8 »	P ak	8 »	6 »
Disapp	16 ›	15 »	D sapp	21 »	15 »

Cer bral blood flow 833 ml/min (7 4 of card ac output)
Card ac output 11 000 ml/min — Total blood volume 5 583 ml — Heart volume 790 ml 380 ml/m

Legend for Fig 13 (opposite page)

Left car art	Ipsilat bulb	Cont alat bulb	
App	3 sec	5 sec	Cardiac output 7 400 ml/min
P k	5 »	7 »	M an c rculation time 10 8 sec
Disapp	13 »	1? »	Total blood volume 5 090 ml
			Heart volume 940 ml 570 ml/m

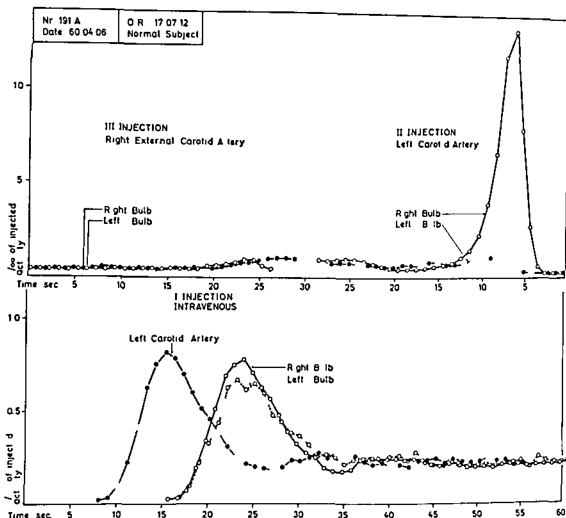


Fig 15 — 43 years

Left car art	Ipsilat bulb	Contralat bulb
App	0 sec	4 sec
Peak	0 »	7 »
Disapp	0 »	16 »

Mean circulation time 9 1 sec
Total blood volume 5 114 ml
Heart volume 780 ml 4?5 ml m²

Legend for Fig 16 (opposite page)

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	3 sec	App	2 sec	? sec
Peak	4 »	6 »	Peak	5 »	5 »
Disapp	13 »	13 »	Disapp	12 »	11 »

Cerebral blood flow 1 067 ml/min (11 5 of cardiac output)
Cerebral pool volume 130 ml (2 4 of total blood volume)
Cardiac output 9 300 ml/min
Mean circulation time 7 3 sec
Total blood volume 5 337 ml
Heart volume 725 ml 370 ml/m²

Legend for Fig 17 (opposite page)

Right car art	Ipsilat bulb	Contralat bulb
App	3 sec	4 sec
Peak	6 »	6 »
Disapp	13 »	9 »

Cardiac output 8 000 ml/min
Mean circulation time 6 8 sec
Total blood volume 4 878 ml
Heart volume 810 ml 450 ml/m²

III INJECTION
Right Carotid Artery

I INJECTION
INTRAVENOUS

II INJECTION
Left Carotid Artery

CAROTID ARTERY

RIGHT BULB
LEFT BULB

Time sec.

Fig 16 26 years

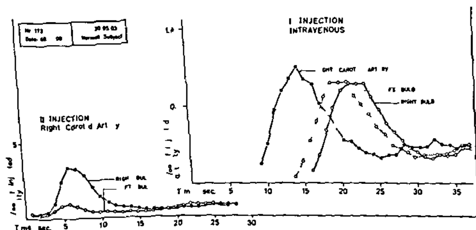


Fig 17 0 years

Nr 197 A | Date 60 04 29 | S L 20 04 11 | Normal Subject

III INJECTION Right Carotid Artery

I INJECTION INTRAVENOUS

II INJECTION Left Carotid Artery

Left Carotid Artery

Right Bulb

Left Bulb

Time sec.

Fig 18

40 years

IV INJECTION Right Carotid Artery

II INJECTION Left Carotid Artery

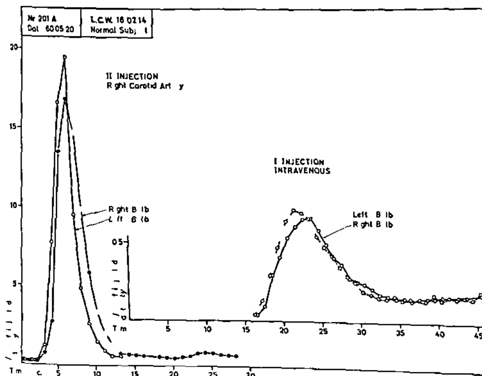
Right Bulb

Left Bulb

Time sec

Fig 19

33 years



F g 20

44 years

Right car art	Ips lat bulb	Contralat bulb
App	3 sec	3 sec
Peak	6	6 »
Disapp	13	12 »

Cerebral blood flow 866 ml/min (10 4 % of car d ac output)
Card ac output 8 300 ml/min
Total blood volum 5 380 ml
Heart volume 680 ml 410 ml/m

Legend for Fig 18 (opposite page)

Right car art	Ips lat bulb	Contralat bulb	Left car art	Ips lat. bulb	Contralat. bulb
App	2 s c	0 sec	App	3 sec	2 sec
P ak	5 »	0 »	Peak	6 »	5 »
Disapp	13	0 »	Disapp	15 »	14

Cer br l blood flow 671 ml min (8 2 of cardiac output)
Ce b al pool volume 96 ml (1 5 of total blood volume)
Card ac output 8 200 ml/min
Mean circul t on t me 8 6 sec

Total blood volume 6 512 ml
Heart olume 850 ml 390 ml/m

Leg nd for Fig 19 (opposite page)

R ght car art	Ips lat bulb	Contralat bulb	Left car art	Ips lat bulb	Contralat bulb
App	4 sec	5 sec	App	4 sec	6 sec
Pe k	7 »	8 »	Peak	7 »	8 »
D sapp	16 »	15 »	Disapp	15 »	14 »

Ce bral blood flow 971 ml min — Total blood volume 5 240 ml — Heart volume 9/0 ml 430 ml/m

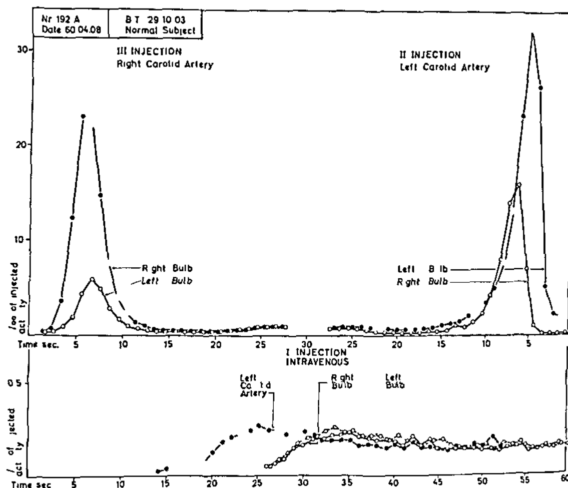


Fig 21 31 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	2 sec	4 sec	App	2 sec	4 sec
Peak	5 »	7 »	Peak	5 »	6 »
Disapp	14 »	13 »	Disapp	17 »	14 »

Cerebral blood flow 791 ml/min (9 7 of cardiac output)
Cerebral pool volume 91 ml (1 5 % of total blood volume)
Cardiac output 8 200 ml/min Total blood volume 6 156 ml
Mean circulation time 6 9 sec Heart volume 840 ml 390 ml/m

Legend for Fig 22 (opposite page)

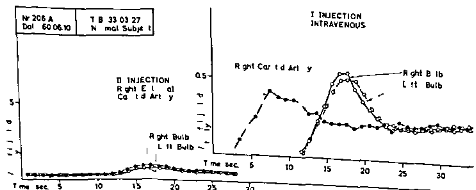
Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	2 sec	4 sec	App	2 sec	3 sec
Peak	5 »	6 »	Peak	4 »	6 »
Disapp	13 »	9 »	Disapp	12 »	13 »

Cerebral blood flow 943 ml/min (15 5 of cardiac output)
Cerebral pool volume 114 ml (3 5 of total blood volume)
Cardiac output 6 100 ml/min Total blood volume 3 265 ml
Mean circulation time 7 3 sec Heart volume 410 ml 280 ml/m

N 194 A Da 60 04 20
D I 32 03 07 No mal S bj t
II INJECTION L ft Car t d A t y
I INJECTION INTRAVENOUS
R ght Ca ot d Artery
R ght Bulb
Left B lb
L ft Bulb
R ght B lb
R ght Bulb L ft B lb
T me sec.

F g 22

28 years



F g 23

27 years

Cardia output 9 300 ml m n
M an cir ulat n t m 4 8 sec

Total blood volume 4 267 ml
Heart volume 730 ml 430 ml m

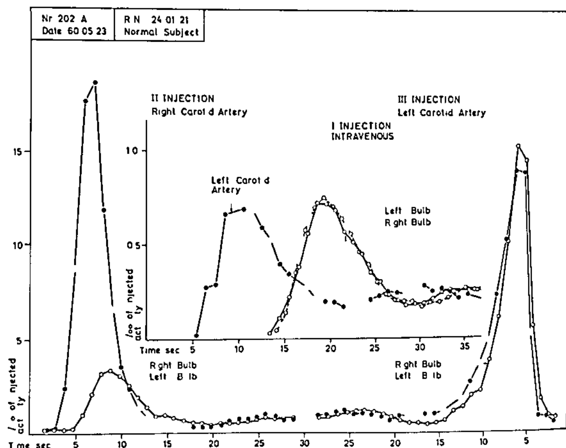


Fig 24

36 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	5 sec	App	3 sec	3 sec
Peak	7 »	9 »	Peak	6 »	6 »
Disapp	14 »	15 »	Disapp	15 »	15 »

Cerebral blood flow 948 ml/min (13 1 % of cardiac output)
Cerebral pool volume 152 ml (3 2 % of total blood volume)
Cardiac output 7 200 ml/min — Total blood volume 4 739 ml
Mean circulation time 9 6 sec — Heart volume 660 ml 400 ml/m²

Acknowledgement

The support received for this work grant H 3219 from the National Institute of Health U S Public Health Service is gratefully acknowledged We also wish to thank Docent G Porjé who has greatly facilitated our investigation

SUMMARY

The cerebral blood flow blood volume and circulation time through the brain were investigated with labelled radioactive erythrocytes in 34 healthy males The time intervals of appearance, peak concentration and disappearance in the jugular bulbs were determined

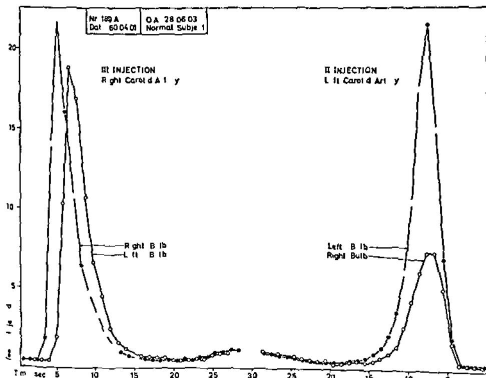


Fig 25

32 years

Right car art	Ipsilat bulb	Contralat bulb	Left car art	Ipsilat bulb	Contralat bulb
App	3 sec	5 sec	App	4 sec	4 sec
Peak	5 »	7 »	Peak	7 »	7 »
Disapp	14	16 »	Disapp	15 »	14 »

Cerebral blood flow /81 ml/min – Total blood volume 4 997 ml — Heart volume 5 0 ml 320 ml/m²

from dilution curves obtained after injection into the carotid arteries The variations were found to be small and no correlation was obtained between the cardiac output and the cerebral blood flow or between the latter and the age of the subjects

ZUSAMMENFASSUNG

Die zerebrale Blutzirkulation die zerebrale Blutmenge und die Umlaufzeit des Blutes durch das Gehirn wurden mit radioaktiven Erythrozyten bei 34 gesunden Männern untersucht Die Zeitabstände zwischen dem Auftreten der höchsten Konzentration und dem Verschwinden in den jugularen Bulben wurden aus Verdünnungskurven nach Injektion in die A caro- tis bestimmt Die Schwankungen sind bei normalen Personen offenbar sehr gering Keine Korrelation wurde zwischen dem Herz Minutenvolumen und dem zerebralen Blutzirkulation oder zwischen dem letzteren und dem Alter der Personen gefunden

RÉSUMÉ

Le débit sanguin cérébral, le volume sanguin et les temps de circulation à travers le cerveau ont été étudiés sur 34 sujets masculins en bonne santé au moyen d'érythrocytes marqués radioactifs. Les intervalles de temps d'apparition, de concentration maximale et de disparition dans les golfes des jugulaires ont été déterminés à partir des courbes de dilution après injection dans les artères carotides. Les variations semblent très minimes chez les sujets normaux. On n'a pas trouvé de corrélation entre le débit cardiaque et le débit cérébral, ni entre celui-ci et l'âge des sujets.

REFERENCES

ANDERSSON, B. J.: Studies on the circulation in organic systems with applications to indicator methods. Trans. Roy. Inst. Technology (Sthlm) (1957) No. 114.

EDWARDS, N. A.: Anatomic variations of the cranial venous sinuses. Arch. Neurol. Psychiat. 26 (1931): 801.

GREITZ, T.: Radiologic study of the brain circulation by rapid serial angiography of the carotid artery. Acta radiol. (1956) Suppl. No. 140.

HELPS, E. P. W. and MC DONALD, D. A.: Observations on laminar flow in veins. J. Physiol. 124 (1954): 124.

MONIZ, E.: Sur la vitesse du sang dans l'organisme. Ann. Méd. 32 (1932): 193.

NYLIN, G.: Estimation of cerebral blood flow and cerebral blood pool by aid of labeled erythrocytes. *In* Cerebral vascular diseases. Ed. by Wright and Millikan. Grune and Stratton, New York, 1958.

— and BLOMER, H.: Studies on distribution of cerebral blood flow with thorium B labeled erythrocytes. Circulat. Res. 3 (1955): 79.

— and HEDLUND, S.: Blood flow and pool in heart, lungs and brain. *In* Circulation. Proc. Harvey Tercentenary Congress. Ed. by John Mc Michael. Blackwell's, Oxford, 1958.

— — and REGNSTROM, O.: Studies of the cerebral circulation with labeled erythrocytes in healthy man. To be published in Circulation Res. (1961).

— BLOMER, H., JONES, H., HEDLUND, S. and RYLANDER, C. G.: Further studies on the cerebral blood flow with thorium B labelled erythrocytes. Brit. Heart J. 18 (1956): 385.

— SILVERSKIOLD, B. P., LOFSTEDT, S., REGNSTROM, O. and HEDLUND, S.: Studies on cerebral blood flow in man, using radioactive labeled erythrocytes. Brain 83 (1960): 293.

SCHURR, P. H. and WICKBOM, I.: Rapid serial angiography. Further experience. J. Neurol. 15 (1952): 110.

SHENKIN, H., HARMEL, M. and KETY, S.: Dynamic anatomy of the cerebral circulation. Arch. Neurol. Psychiat. 60 (1948): 240.

TONNIS, W. und SCHIEFER, W.: Zirkulationsstorungen des Gehirns im Serienangiogram. Springer Verlag, Berlin, Gottingen, Heidelberg, 1959.

FROM THE RESEARCH LABORATORIES OF SCHERING A (BERLIN DEUTSCHLAND

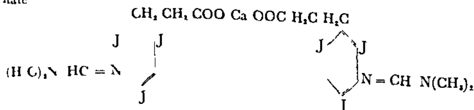
PHARMACOLOGICAL PROPERTIES AND EXCRETION KINETICS OF SOLU BILOPTIN

by

K H KIMBEL and H LANGECKER

The fact that Biloptin like virtually all other compounds used for oral cholecystography and cholangiography has a disagreeable taste prompted us to supply this new contrast medium (sodium β (3 dimethylamino methyleneamino 2 4 6 triiodophenyl) propionate) in capsules instead of tablets It is well known that a certain percentage of patients and e pecially those with gastrointestinal disorders are unable to swallow capsules and we therefore decided to look for a tasteless derivative of Biloptin® (B) that could be administered in the form of a suspension The calcium salt Solu Biloptin® (SB) which is sparingly oluble in water surpassed all other tested compounds in this respect and surprisingly exhibited excellent roentgenographic properties besides being well tolerated (SALTZMAN)

Chemical properties (according to figures supplied by Dr W Neudert) Calcium bis β (3 dimethylamino methyleneamino 2 4 6 triiodophenyl) propionate



Submitted for publication 6 December 1960

RÉSUMÉ

Le débit sanguin cérébral le volume sanguin et les temps de circulation à travers le cerveau ont été étudiés sur 34 sujets masculins en bonne santé au moyen d erythrocytes marqués radioactifs Les intervalles de temps d apparition, de concentration maximale et de disparition dans les golfes des jugulaires ont été déterminés à partir des courbes de dilution après injection dans les artères carotides Les variations semblent tres minimes chez les sujets normaux On n'a pas trouvé de corrélation entre le débit cardiaque et le débit cérébral, ni entre celui ci et l âge des sujets

REFERENCES

ANDERSSON B J Studies on the circulation in organic systems with applications to indicator methods Trans Roy Inst Technology (Sthlm) (1957) No 114

EDWARDS N A Anatomic variations of the cranial venous sinuses Arch Neurol Psychiat 26 (1931), 801

GERLITZ L Radiologic study of the brain circulation by rapid serial angiography of the carotid artery Acta radiol (1956) Suppl No 110

HELPS E P W and MC DONALD D A Observations in laminar flow in veins J Physiol 124 (1954) 124

MONIZ E Sur la vitesse du sang dans l organisme Ann Med 32 (1932) 193

NYLIN G Estimation of cerebral blood flow and cerebral blood pool by aid of labeled erythrocytes *In* *Cerebral vascular diseases* *Ed by Wright and Millikan* Grune and Stratton New York 1958

— and BLOMER H Studies on distribution of cerebral blood flow with thorium B labeled erythrocytes Circulat Res 3 (1955) 79

— and HEDLUND S Blood flow and pool in heart lungs and brain *In* Circulation Proc Harvey Tercentenary Congress Ed by John Mc Michael Blackwell s Oxford 1958

— — and REGNSTROM O Studies of the cerebral circulation with labeled erythrocytes in healthy man To be published in Circulation Res (1961)

— BLOMER H, JONES H HEDLUND S and RYLANDER C G Further studies on the cerebral blood flow with thorium B labelled erythrocytes Brit Heart J 18 (1956) 385

— SILFVERSKIOLD B P LOFSTEDT S, REGNSTROM O and HEDLUND S Studies on cerebral blood flow in man using radioactive labeled erythrocytes Brain 83 (1960) 293

SCHURR P H and WICKBOM I Rapid serial angiography Further experience J Neurol 15 (1952) 110

SHENKIN H HARMEL M and KETY S Dynamic anatomy of the cerebral circulation Arch Neurol Psychiat 60 (1948) 240

TONNIS W und SCHIEFER W Zirkulationsstorungen des Gehirns im Serienangiogram Springer Verlag Berlin Gottingen Heidelberg 1959

Table 2

Excretion of labelled Biloptin (B) and Solu Biloptin (SB) (prepared by Dr Schulze) in bile of rats weighing between 100 and 120 g after intraduodenal application of 100 mg/kg bodyweight of the compounds The figures represent percentages of the administered dose calculated from the I^{131} content in the bile

Compound	Number of animals	0—1/2 hr	1/2—1 hr	1—2 hrs	2—3 hrs	3—4 hrs	Total
Solu Biloptin[1]	18	7 1	14 0	26 2	17 4	9 3	74 0
Solu Biloptin[2]	9	5 5	17 8	30 0	18 5	8 9	80 7
Biloptin[3]	12	6 3	15 7	32 0	18 3	9 6	81 9
Biloptin[4]	10	16 7		29 6	23 1	11 7	81 1

1) 2 % suspension in 10 gum acacia
2) In the form of the commercial preparation (4 % micronized suspension with some additives)
3) and 4) 2 solution of the sodium salt

Effects on circulation and respiration Intravenous injections of 4 ml of a saturated solution of SB in Ringer s solution into cats anesthetized with Pernocton did not change the blood pressure or respiration rate In the isolated frog heart preparation (Straub) the lowest concentration which caused a bradycardiac and a negative inotropic effect was identical with that found for B (10 ³) Concentrations down to 10 ⁵ induced a vasodilatation in the L norepinephrine pretreated rabbit s ear vein

Influence on smooth muscle Concentrations down to 2 10 were found ineffective in the isolated guinea pig small intestine the $BaCl_2$ spasm was inhibited partially at 2 10 and totally at 10 ⁴ the same concentration antagonizing the spasm induced by lentine and histamine In the isolated rabbit small intestine concentrations from 10 brought about a decrease in amplitude while tone and frequency remained unchanged In the rabbit uterus no effect was seen up to 1 5 10 ⁴ Beginning with 7 5 10 the effect of epinephrine was inhibited

Excretion kinetics

Experiments in rats We have shown in an earlier paper (Harwart Kimbel Langecker and Willenbrink (1959) that more than 80 % of a single intraduodenal dose of 100 mg B (sodium salt)/kg bodyweight is excreted within 4 hours in the bile of rats This route of administration is required in bile fistula experiments in rats because of the impaired gastric peristalsis after laparotomy Furthermore larger variations in absorption which due to different gastric evacuation time would occur after oral administration are thus avoided The results of these experiments are compared with similar

Table 1

Comparison of acute toxicity of B and SB in mice weighing between 18 and 22 g and rats weighing 100 to 120 g LD_{50} was calculated according to KARBER

Species	B = Sodium salt Route of administration			SB — Calcium salt Route of administration	
	Intravenous solution	Intra peritoneal solution	Peroral solution	Intra peritoneal suspension	Peroral suspension
Rat	0 3—0 4	0 37	2 8—3 2	0 43	1 5—3 0
Mouse	0 3	0 35	1 5	0 3	1 0

$C_{24}H_{24}J_6N_4O_4Ca$, has a molecular weight of 1 234 and an iodine content of 61 7 % The colorless and slightly bitter tasting microcrystalline compound melts at 298 to 302° C and has the following solubilities at 37° C water 0 35 g/100 ml, normal saline (0 9 %) 0 46 g/100 ml, plasma ~ 2 3 g/100 ml, olive oil ~ 1 8 g/100 ml

It is fairly soluble in $HCCl_3$ (in presence of traces of C_2H_5OH) and in glacial acetic acid, readily soluble in dimethyl formamide and dimethylsulphoxide and insoluble in acetone and ether Ultraviolet absorption ε_{61} = 25 800 and ε_{234} = 74 300 (methyl alcohol), ε_{233} = 71 900 (water)

Pharmacologic properties

Acute and chronic toxicity In toxicity SB closely resembles the sodium salt (B) The LD 0 of both compounds as determined in rats and mice are presented in Table 1

SB seems to be slightly better tolerated in rats than B on intraperitoneal injection although the corresponding values in mice are identical The subacute toxicity was tested in 10 rats (90 to 110 g bodyweight) receiving 8 doses of 200 mg SB/kg bodyweight as a 20 % suspension in gum acacia orally during 10 days They gained about 30 % in bodyweight and looked normal The same dose given to 10 rats of the same weight 15 times during 19 days did not change the normal weight increase of about 37 % Microscopic examination of the liver and kidney did not reveal any pathologic changes, the same was true of the urine analysis Three dogs weighing between 8 1 and 10 5 kg received 200 mg SB/kg bodyweight in capsules 14 times during 17 days and showed no signs of incompatibility nor changes in bodyweight blood or urine

Local compatibility A saturated solution of SB in Tyrode s solution is well tolerated when injected intramuscularly in dogs (0 5 ml) rabbits (0 5 ml) and rats (0 1 ml), a subcutaneous injection of 0 1 ml into rabbits ear or guinea pigs abdomen produced no irritation Instillation into the rabbit eye was also well tolerated

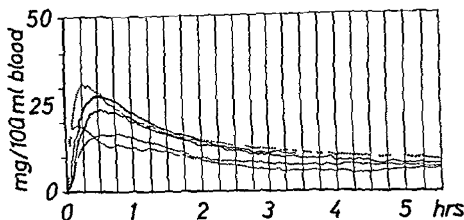


Fig 2 Recording of I concentration in the peripheral blood of albino rats weighing 200 to 250 g measured in an extracorporeal shunt between the carotid artery and the external jugular vein of one rat Operation under ether anesthesia experiment without anesthesia The continuous curves represent Solu Biloptin and the dotted curves Biloptin

that in the latter method the integral over the observation time is shown while the continuous recording reflects the concentrations present in the bile over a very short time limited only by the time constant inherent in the counting process and the chart recorder

The intravenous injection of 100 mg SB (as a 2 % suspension in gum acacia) is well tolerated by rats and results in biliary excretion rates which closely resemble those obtained with B From these results we have drawn the conclusion that the solubility of SB in blood at body temperature must be higher than in water which has been confirmed by the solubility determinations given before The excretion data are presented in Table 3

Comparing the data obtained from the intraduodenal and intravenous administration it is surprising to find that there are differences only in the values for the first half hour while the total output after three hours is of the same order This observation speaks well for an excellent absorption of both compounds through the intestinal wall and was expected for the highly water soluble sodium salt On the other hand the amount of water present in the rat intestine under normal conditions is not sufficient to dissolve 10 mg of the SB administered Since the solubility of SB in 0 9 % saline at 37° C was found to be 0 46 % 2 2 ml of saline would be necessary to dissolve this amount In spite of the fact that due to the continuous removal of the dissolved fraction of SB by absorption the dissolution of the remainder would be facilitated, we would still have to find a slower absorption rate for SB This however is not the case

The excretion of SB in bile reflects the absorption process only indirectly

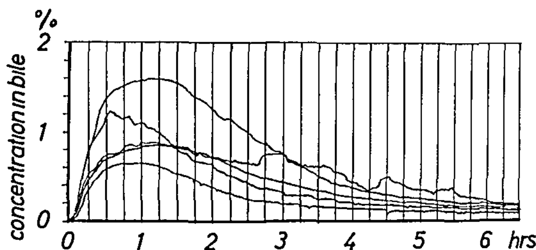


Fig 1 Continuous recordings of radioactivity in bile fistula outflow of rats that received 100 mg/kg bodyweight of SB I^{131} by intraduodenal injection at time 0 The system was calibrated by a 2 % solution of SB I^{131}

ones in bile fistula rats that received the same dose of SB as a suspension in gum acacia (18 animals) or in a micronized form (9 animals) It is evident from Table 2 that the rate of biliary excretion in rats is practically identical for both compounds

With a new technique which has previously been described in detail (KIMBEL 1958) the absolute concentration of the opacifying element, i e the iodine concentration of a I^{131} labelled preparation, was recorded continuously in the bile passing the polythene tube of the bile fistula From the five curves shown in Fig 1 it is evident that the maximum of I^{131} concentration in the bile is attained between 30 and 90 minutes after administration with values ranging from 0 6 to 1 6 % SB The apparent discrepancy between these figures and the amounts excreted over the collecting periods in Table 2 which reach the maximum between 1 and 2 hours, may be explained by the fact

Table 3

Excretion of labelled B and SB in the bile of rats weighing between 100 and 120 g given in percentages of administered dose calculated from the I^{131} content in the bile after intravenous injection of 100 mg/kg bodyweight as sodium salt (B) or gum acacia suspension (SB)

	Animal No	0—1/2	1/2—1	1—2	2—3 hrs	Total
Intravenous injection						
Solu Biloptin	10	14 7	18 7	21 2	16 0	70 6
Biloptin	9	26 5		23 0	14 2	63 7
Injection into the portal vein						
Solu Biloptin	5	8 6	13 9	19 6	16 4	58 5

Table 5

Excretion of Ca45 in the bile of rats weighing from 100 to 150 g after the intraduodenal administration of 100 mg/kg SB labelled with Ca45 as 2 % suspension in 10 % gum acacia and an equivalent amount of 45CaCl2 prepared in the same way given as percentages of the administered dose

Compound	Animal No	0—1/2	1/2—1	1—2	2—3	3—4 hrs	Total
SB — Ca4	10	0 2	0 5	0 6	0 4	0 2	1 9
	5	0 03	0 07	0 2	0 2	0 5	1 0
45CaCl	5	0 28	0 20	0 22	0 16		0 9

Instead of a ratio of 1 1 for equimolar amounts of Ca and I131 Biloptin amon the samples taken 20 minutes after intraduodenal administration showed ratios of 0 93, 0 69 0 74 and 0 68 These figures indicate that during this interval a fraction of radioactivity represents a transformation product of SB which contains no Ca 20 minutes later, i e 40 minutes after injection the respective values are 0 88, 1 00 and 1 34 which means that most of the labelled material is now being absorbed in the unchanged form

Besides the changes observed for B which are discussed in the earlier cited report (HARWART KIMBEL LANGECKER and WILLENBRINK) SB seems to undergo a further change in the liver, insofar as practically all the Ca is removed from the molecule Hardly 2 % Ca4 of a dose of 100 mg/kg SB Ca45 will be found in rat bile over a period of 4 hours compared with nearly 75 % of the I131 labelled compound The data together with those from a control experiment in which equimolar amounts of 45CaCl have been administered are presented in Table 5

We roughly estimated the solubility of SB in olive oil in order to exclude an absorption via a solution in lipoid material present in the intestine and found that 5 ml of olive oil are not sufficient to dissolve 10 mg SB as used in rats This finding excludes the possibility of its absorption in a dissolved form although it may still pass through the intestinal wall as an emulsion In order to clarify the matter we administered 100 mg SB/kg to 5 rats with abdominal lymphatic fistulae (according to BOLLMANN) by intraduodenal injection As shown in Table 6 the small amount of the compound present in the lymph cannot explain the good intestinal absorption of the SB Furthermore these results do not give an explanation for the lower SB level in the portal vein blood which might have been caused by an additional lymphatic transport

Table 6

Transport of SB I through abdominal lymphatics in 5 rats weighing between 235 and 308 g shown as percentage of the administered dose collected from abdominal lymphatic fistulas over a period of 24 hours

	Animals numbered 1	2	3	4	5	Average
I nt of administer d dose	0 8	1 0	0 8	1 7	0 9	1 0

Table 4

Absolute and comparable concentrations in portal vein blood of rats weighing between 225 and 250 g
The maximum values are underlined

Time after injection	I^{131} concentration in portal vein blood of 2 rats after intraduodenal injection of 100 mg/kg bodyweight of SB I^{131}				Ca^{45} concentration in portal vein blood of 4 rats after intraduodenal injection of 8.8 mg/kg bodyweight of $^{45}CaCl_2$, corresponding to the Ca content of SB			
min	1		2		1	2	3	4
	mg %	% of dose/ml	mg %	% of dose/ml	% of administered dose/ml			
10	12.2	0.47	15.3	0.57	0.11	0.10	0.09	0.05
20	15.4	0.59	14.1	0.54	0.17	0.23	0.22	0.10
30	17.3	0.66	13.8	0.53				
40	13.5	0.52	11.4	0.44	0.26	0.28	0.27	0.13
50	12.8	0.49	11.8	0.45				
60	11.7	0.45	11.2	0.43	0.29	0.27	0.18	0.23

In order to obtain a closer insight into the absorption mechanism the blood level of I^{131} labelled SB was studied in the peripheral and portal vein blood. Fig. 2 shows that the continuously recorded level in the peripheral blood rises sharply a few minutes after the intraduodenal introduction of 100 mg SB/kg bodyweight attaining a maximum of 15 to 30 mg/100 ml within 30 to 60 minutes. The most important finding is the observation that, considering the biologic variation, there is no significant difference in the slope and maximum between the curves obtained for B and SB.

The concentrations in the portal vein blood which are given in Table 4 were calculated from individual samples taken every 10 minutes over a period of 1 hour. As regards their maximum the levels satisfactorily correspond with those found in the peripheral blood (Fig. 2). The absolute level in the portal vein blood was unexpectedly found to be lower than the arterial blood level. We may conclude from these experiments that the calcium salt SB and the sodium salt B are equally well absorbed by the rat intestine. In view of the poor solubility of the calcium salt in water this is rather surprising and may possibly be due to its transformation into a water soluble form or to some special absorption mechanism, e.g. absorption via the lipoid phase or as particulate matter.

In an endeavour to study the first possibility SB was labelled with I^{131} as well as with Ca^{45}. If the unchanged calcium salt were absorbed, the specific activity would remain the same for I^{131} and Ca^{45}. In order to exclude the possibility that the Biloptin anion and the liberated Ca would have the same absorption rate, simulating the presence of unchanged SB, the Ca^{45} level in the portal vein blood was determined after the administration of an equivalent amount of $^{45}CaCl_2$ under comparable conditions. As demonstrated in Table 4 only 1/3 to 1/2 of an equivalent dose of $^{45}CaCl_2$ is absorbed

Table 5

Excretion of Ca^{45} in the bile of rats weighing from 100 to 130 g after the intraduodenal administration of 100 mg/kg SB labelled with Ca^{45} as 2 % suspension in 10 gum acacia and an equivalent amount of $^{45}CaCl_2$ prepared in the same way given as percentages of the administered dose

Compound	Animal No	0—1/2	1/2—1	1—2	2—3	3—4 hrs	Total
SB — Ca^{45}	10	0 2	0 5	0 6	0 4	0 2	1 9
	5	0 03	0 07	0 2	0 2	0 5	1 0
^{45} CaCl	5	0 28	0 20	0 22	0 16		0 9

Instead of a ratio of 1 1 for equimolar amounts of Ca and I^{131} Biloptin anion the samples taken 20 minutes after intraduodenal administration showed ratios of 0 93 0 69 0 74 and 0 68 These figures indicate that during this interval a fraction of radioactivity represents a transformation product of SB which contains no Ca 20 minutes later, i e 40 minutes after injection, the respective values are 0 88 1 00 and 1 34 which means that most of the labelled material is now being absorbed in the unchanged form

Besides the changes observed for B which are discussed in the earlier cited report (HARWART KIMBEL LANGECKER and WILLENBRINK) SB seems to undergo a further change in the liver, insofar as practically all the Ca is removed from the molecule Hardly 2 % Ca^{45} of a dose of 100 mg/kg SB Ca^{45} will be found in rat bile over a period of 4 hours compared with nearly 75 % of the I^{131} labelled compound The data together with those from a control experiment in which equimolar amounts of $^{45}CaCl_2$ have been administered are presented in Table 5

We roughly estimated the solubility of SB in olive oil in order to exclude an absorption via a solution in lipoid material present in the intestine and found that 5 ml of olive oil are not sufficient to dissolve 10 mg SB as used in rats This finding excludes the possibility of its absorption in a dissolved form although it may still pass through the intestinal wall as an emulsion In order to clarify the matter we administered 100 mg SB/kg to 5 rats with abdominal lymphatic fistulae (according to BOLLMANN) by intraduodenal injection As shown in Table 6 the small amount of the compound present in the lymph cannot explain the good intestinal absorption of the SB Furthermore these results do not give an explanation for the lower SB level in the portal vein blood which might have been caused by an additional lymphatic transport

Table 6

Transport of SB I^{131} through abdominal lymphatics in 5 rats weighing between 235 and 308 g shown as percentages of the administered dose collected from abdominal lymphatic fistulas over a period of 24 hours

	Animals numbered 1	2	3	4	5	Average
Per cent of administered dose	0 8	1 0	0 8	1 7	0 9	1 0

Table 7

Excretion of I^{131} in the bile and urine of 2 rabbits after intraduodenal injection of 100 mg labelled SB/kg bodyweight. At the beginning of the experiment the animals were given 50 ml water. After each withdrawal the bladder was rinsed with 4 ml 0.9 % NaCl injected through an indwelling catheter. The figures represent the percentage cumulative excretion of the administered dose

	Animal No	0—1/4	0—1/2	0—1	0—2	0—3	0—4	0—24 hrs
Bile	1	0.1	0.4	1.0	2.0	3.2	4.3	10.2
	2	0.1	0.2	0.6	1.3	1.7	1.9	4.3
Urine	1	0.1	0.2	0.8	2.4	3.9	7.1	63.1
	2	0.8	1.4	2.3	5.0	8.4	10.4	48.6

Surveying our results with respect to the absorption mechanism of SB it may be stated that SB passes through the portal vein and is absorbed preferentially as a Ca salt. The mechanism facilitating its passage through the intestinal wall remains obscure but transport by the lipoid phase could be excluded. The assumption that solubilizing compounds in the intestinal juices are responsible for the fast absorption of SB is supported by an experiment in which we were able to demonstrate that SB has a solubility of about 90 % in rat intestinal juices of a pH of 6.7 to 7.0.

In accordance with the results obtained with B, the fraction of SB or its metabolic products excreted in the urine is small due to the rapid elimination of the compound via the bile. Three hours after the intravenous injection of 100 mg SB/kg, 4.2 % of the administered dose was found in the urine while 6.6 % was excreted within 4 hours after oral administration (animals Nos 5 and 4 respectively, metabolic cage). Since in these experiments the flow of the bile into the intestinal lumen was not interrupted or deviated, an enterohepatic circulation cannot be excluded, however, in our experiments with the sodium salt (B) we have been able to show (HARWART et coll.) that reabsorption occurs to a minor degree only. In an experiment run over a period of 24 hours 31.1 % of the administered dose was found in the faeces and 19.6 % in the urine. From a clinical point of view it seems to be of interest that after ligature of the common bile duct in rats the urinary excretion within 4 hours was as high as 34.1 % of the dose administered by intravenous injection.

Table 8

Excretion of 100 mg SB/kg as a 2 % suspension in 10 % gum acacia given by stomach tube to 2 dogs. The iodine content of the bile and urine was determined chemically according to LANGECKER. *The figures represent the percentage of the administered dose*

Animal No	Excretion in bile		Excretion in urine	
	0—4 hrs	0—24 hrs	0—4 hrs	0—24 hrs
1	35	88	2.2	6.1
2	63	88.6	2.9	6.1

Table 9

Urinary excretion of 3 g SB in healthy volunteers Figures calculated from the iodine content in urine determined chemically according to LANGECKER

Volunteer No	Cumulative excretion in % of administered dose 0—2 hrs	0—4 hrs	0—8 hrs	0—24 hrs
1		16 6	23 4	48 4
	6 9	12 7	21 3	
2		9 0	21 7	46 7
	6 4	13 0	23 7	
3		8 9	27 9	42 2
4	5 8	12 6	28 1	
5	7 3	17 9	33 4	
6	8 3	13 4	23 2	
7	4 8	12 6	27 6	

Experiments in rabbits It is generally recognized that rabbits are not the animals of choice in the evaluation of biliary contrast media In an experiment with 2 animals weighing 2 1 to 2 2 kg the gallbladder was ligated during the preparation of an acute bile fistula In one case the excretion of I^{131} in the urine was ten times as high as that in the bile while in the other animal the bile urine coefficient was about 0 16 The reason for the different behaviour of rabbits necessitates further investigation (Table 7)

Experiments in dogs Two dogs (13 kg and 16 kg) with a permanent bile fistula (according to the method of HARWART KIMBEL and LANGECKER (1959) received 100 mg SB/kg as a 2 % suspension in 10 % gum acacia orally During a period of 24 hours both animals excreted 88 % of the administered dose in the bile The figures are given in Table 8 The amount of iodine excreted within 4 hours in dog No 2 agrees well with the data presented for rats

Experiments in man Since we had no opportunity of studying the excretion of SB in clinical cases of acute bile fistulae we had to confine ourselves to the study of the excretion of SB in the urine of healthy volunteers The data of the experiment in which 3 g SB were given orally to the fasting subjects in the early morning are presented in Table 9 It may be seen that 42—48 % was excreted in the urine within 24 hours If we assume that the compound excreted in the bile is poorly reabsorbed as it is in rats we can deduce that about the same amount was excreted in the bile When administered to clinical cases with abundant free gastric hydrochloric acid the possible formation of Biloptin acid and its subsequent transformation into the sodium salt due to the alkaline reaction of the duodenum must be considered A model experiment in which 1 mmol = 1 234 g SB were homogenized in 5 mmol 0 1 N HCl at 37 C for 10 min resulted in a transformation into the acid of about 54 %

SUMMARY

Intestinal absorption urinary and biliary excretion, toxicity and common pharmacologic properties of a tasteless derivative of Biloptin have been investigated in rats dogs and man It was found that Solu Biloptin has the same favourable properties as Biloptin with respect to tolerability absorption and biliary excretion In spite of its poor solubility in water Solu Biloptin is absorbed at least as quickly as Biloptin An attempt is made to elucidate its absorption mechanism

ZUSAMMENFASSUNG

Die Resorption im Darm, Ausscheidung in Galle und Harn Toxizitat und allgemeine pharmakologische Eigenschaften einer geschmacklosen dem Biloptin verwandten Verbindung wurde an Ratten Hunden und beim Menschen gepruft Es ergab sich dass Solu Biloptin die gleichen guten Eigenschaften wie Biloptin im Hinblick auf Vertraglichkeit Resorption und Gallenausscheidung aufweist Trotz seiner geringen Wasserloslichkeit wird es zumindest ebensogut resorbiert wie Biloptin Es wurde versucht den Resorptionsmechanismus von Solu Biloptin aufzuklaren

RESUMÉ

Les auteurs ont étudie sur le rat le chien et l homme l absorption intestinale l excretion urinaire et biliaire la toxicite et les propriétes pharmacologiques usuelles d un dérivé insipide du Biloptin Ils ont constaté que le Solu Biloptin est aussi bien toléré absorbé et excrété par voie biliaire que le Biloptin Malgré sa faible solubilité dans l eau le Solu Biloptin est absorbé au moins aussi vite que le Biloptin Les auteurs se sont efforces d élucider le mecanisme de son absorption

REFERENCES

BOLLMAN J L CAIN J C and GRINDLAY J H Techniques for the collection of lymph from the liver small intestine or thoracic duct of the rat J Lab Clin Med 33 (1948) 1349

HARWART A KIMBEL K H und LANGECKER H Die Beurteilung von Resorption und Ausscheidung der Gallenkontrastmittel Arch exper Path Pharm 230 (1957) 567

— — — *und* WILLENBRINK J *β (3 dimethylamino methylen amino 2 4 6 trijodphenyl) propionsaure* als Gallenkontrastmittel Arch exper Path Pharm 237 (1959) 186

KIMBEL K H Vorteile radioaktiv markierter Substanzen bei Clearance und Verteilungsversuchen 3 Sympos Radioisotope in Klinik und Forschung Urban u Schwarzenberg Munchen u Berlin 1958

LANGECKER H Die Verbrennung von Korperflussigkeiten in Sauerstoffatmosphare und ihre Anwendung zur Jodbestimmung in kontrastmittelhaltigen Flussigkeiten Klin Wschr 37 (1959) 471

SALTZMAN G F Solu Biloptin (SH 530) as a contrast medium for peroral cholegraphy Acta radiol 54 (1960) 417

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CONDENSER CHAMBER DOSEMETER FOR RADIATION MEASUREMENT AT LOW DOSE RATE

by

R Thoraeus

The radiation hazards to which workers may be subjected in various types of radiologic work are today extensively studied and discussed The discussion is based more or less on radiation measurements made by monitoring the radiation received by the individual workers In papers on such measurement results the properties of the instruments used are however not always given and the reader is thus unable to assess the accuracy and reliability of the results

One of the most dominant practical difficulties connected with protection in radiologic work is the fact that the radiation is only gradually attenuated by matter This means that total protection cannot be obtained with a finite thickness of any material The dimensions of protective barriers will thus include consideration of levels

In general when radiation interacts with matter the energy of the beam will primarily be converted into motion of electrons It is these electrons which for example are biologically efficient The process by which the electrons are set in motion is however very complicated In addition the interaction is connected with emission of scattered radiation and as this has lower energy than the primary the total radiation will have a spectral distribution extended more or less in the direction towards lower energy The spectral distribution after the interaction is consequently not the same as it was before, the radiation

Submitted for publication 21 September 1960

quality is degraded It is therefore of importance to use measuring instruments the energy dependence of which is small enough to permit safe measurements, even if the quality (spectral distribution) of the radiation is insufficiently known Reference may be made to the NBS Handbook 51 (2) in which paragraph 11 8 runs as follows 'All instruments for general use should be checked for energy dependence with gamma radiation from Ra or Co 60 and with X rays There should not be more than a 20 per cent variation between 100 keV and 2 MeV Further instrument requirements will be found in paragraphs 16 to 19 of the same handbook

The radiation behind protective barriers is usually not coming from a defined direction The scattered radiation, for example, is arising from the whole irradiated volume of matter, and is thus very diffuse This condition necessarily requires that the radiation detector (ionization chamber) has a sufficiently small direction dependence

There are, finally, two fundamental conditions in the use of ionization chambers the dose rate must be fairly constant over the volume occupied by the chamber, and the chamber must be completely irradiated The last mentioned condition excludes, for example, narrow beams from being measured by chambers the size of which is greater than the cross section of the beam

Exposure dose measurement of low dose rate roentgen radiation in terms of the international roentgen by inclosed ionization chambers was discussed by the author in a previous paper (4) The design and properties of some condenser dosemeters provided with such chambers were then described One of these instruments, designed and constructed by the author as early as 1943, is of particular interest as having a very high sensitivity, yet being of a reasonable size so that it may be conveniently used in both laboratory work and practical inspection Its ionization chamber is cylindrical about 15 cm in length and 7 5 cm in diameter, and is provided with a hollow inner electrode 0 8 cm in diameter It has an enclosed air volume of about 563 cm^3, and a total electrostatic capacitance of about 4 cm The reader is referred to the quoted paper for further details

This cylindric chamber was found to have sufficiently small direction and energy dependencies It was extensively calibrated against a special chamber, a so called drum chamber previously described by the author (3) The drum chamber in turn was directly calibrated against our free air standard chamber in the region of 10 to 165 kV tube voltage, in this same region the variation of its calibration factor was only plus or minus 2 5 per cent

The calibration result of the cylinder chamber is quoted in Table 1 Primary radiation as well as secondary radiation scattered from a wax phantom were used in the calibration The result does not show any systematic changes of sensitivity due to quality of the radiation, and we may therefore be justified in using the average value k = 25 5 μr per volt When this value is used over the whole range of radiation qualities investigated, the maximum error intro

Table 1

Calibration results of chamber without added cap

Additional filter mm*	Tube voltage	Calibration factor in μr per volt	Radiation used
7 Pb	400 kV half wave	26 3	Primary radiation obtained with tube voltage and filtration given
1 Pb	165 kV const. potential	25 7	
Tin filter	165 »	25 3	
0 5 Cu	165 »	25 7	
4 Al	145 »	25 6	
1 Al	100 »	25 2	
0	70 »	25 6	
0	50 »	24 5	
0	50 kV const potential	26 2	Secondary radiation from a wax phantom irradiated by a primary beam obtained with tube voltage and filtration given
0	40 »	25 0	

Average factor 25 5 μr per volt $\pm$ 3 5 per cent

* The inherent filtration of the roentgen tube used at 400 kVp was equivalent to 0 6 mm Cu. At the remaining tube voltages another tube was used the inherent filtration of which was equivalent to only 0 95 mm Al

duced will only be plus or minus 3 5 per cent even if no details of the radiation quality are known In regard to the wide range of qualities used this error may be considered relatively small It may also be compared with accordant observations showing that a change of 5 per cent in the radiation received usually does not perceptibly affect the biologic reactions of the human body

It may be worth mentioning that the sensitivity of the cylindric chamber was later directly calibrated against our free air standard chamber at a tube voltage of 100 kV and an added filter of 4 mm of copper The factor obtained was 25 0 μr per volt This value may be compared with the value of 25 2 μr per volt given in Table 1 for 100 kV and a total filtration of about 2 mm of aluminium The difference is only 0 8 per cent

It appears further from Table 1 that three calibration factors have been obtained at 165 kV tube voltage using the three added filters 0 5 Cu + 1 Al normal tin filter and 1 mm Pb The average of the three factors is 25 6 μr per volt and they all lie within the limits plus or minus 0 8 per cent These observations show that the calibration factor is not affected by the great changes of spectral distribution obtained by such very different filtrations

Due to these properties and to those shown in the previous paper (4) as well as to its reliable and stable performance, this cylinder chamber dosemeter has long been used by the standard laboratory as a substandard against

Table 2

Calibration results of chamber with cap

Primary radiation obtained with the tube voltages given below	HVL in mm Cu of the radiation used	Calibration factor in μr per volt
100 kV	0.1	26.5
140 »	0.35	26.0
175 »	0.9	25.5
200 »	2	25.0
280 »	4.4	25.2
Ra γ	13.3	25.2

Average factor 25.6 μr per volt $\pm$ 2.9 %

which other instruments for inspection of protection are calibrated. In addition, two such instruments are used by the radiation protection inspection section of this institute for checking the sensitivity of their routine instruments. Measurements of the exposure dose rate at a sufficient number of suitably selected positions is the first and usual way of obtaining a survey of the radiation field caused by a radiation emitting source. Dosemeters of the type described above have, in fact, also proved to be very suitable for such surveying.

However, the increasing use of high energy radiation, for example gamma radiation, has raised the question as to whether the cylindric substandard can be used also in this region. It would then be necessary to provide the chamber with a complete enclosure of a suitable material to be sure that equilibrium ionization is measured. For this purpose a cylindrical enclosure of plexiglas was constructed. Its function is the same as that of the graphite cap used with the thimble chamber substandard previously described (1), viz. to provide equilibrium wall thickness. Readings were then taken with and without this enclosing 'cap', using roentgen radiation of tube voltages of 100 to 280 kV, and gamma radiation from the radium standard previously described (5). The exposure dose rate measurement of this radium gamma radiation is based on the substandard also previously described (1, 6) and its calibration against four national free air standard chambers in the region of conventional roentgen radiation and against the cobalt 60 gamma radiation standard of the National Bureau of Standards, Washington, USA. The calibration factors of the cylindric substandard thus obtained are collected in Table 2. The average of the factors in *μr per volt is 25.6 $\pm$ 2.9 per cent, which is very nearly the same as that* given above for the chamber without cap.

It appears that at 100 kV and the light filtration resulting in a half value layer of only 0.1 mm Cu, the attenuation in the added cap just begins to raise the calibration factor perceptibly. Checks taken in the region 50 to 70 kV, and using a total filtration of only about 1 mm Al, have shown that the factor of the

substandard with cap is then 7 to 10 per cent higher than that without cap. To avoid impairment of the accuracy the added cap should accordingly not be used when radiations of energies below 100 kV are to be measured. However, if we permit a total variation in energy dependence of $\pm$ 7 per cent, i. e. well within the recommendations in the NBS Handbook 51 (2), the substandard with cap and with an average factor of about 26.5 μr per volt may be used over the whole energy region from 50 kV and practically to the present upper limit of the official validity range of the roentgen without any particular knowledge of the radiation quality being required. Such a decrease of the measurement accuracy may be accepted when only approximative values are required for example in preliminary studies of a radiation field but not in calibration work in a standard laboratory.

The calibration factors shown in Tables 1 and 2 indicate a rather high sensitivity suitable for measurement of radiations of very low dose rate. However, when instruments of considerably lower sensitivity are to be calibrated it is of great value to be able to reduce the sensitivity of the substandard. This can readily be accomplished by adding a suitable capacitor: this increases the electrostatic capacitance of the unit but does not alter the percentage change of calibration factor with radiation quality. Such a capacitor with amber as the dielectric medium is available for this purpose. It changes the calibration factor of the unit from 25.5 to 680 μr per volt, i. e. an increase of the factor by 26.6 times. The sensitivity is then suitable for calibration of instruments having measurement ranges of 50 to 250 mr.

SUMMARY

A cylindric condenser chamber dosemeter for exposure dose measurement of low dose rate radiations and its calibration results are described. As the chamber has a very low energy dependence it can be used with the same average calibration factor for radiations of energies from 40 kV and practically up to the present upper limit of the official validity range of the international roentgen unit.

ZUSAMMENFASSUNG

Ein zylindrischer Kondensatorkammerdosismesser für Messung von Bestrahlungsdosen von Strahlen mit geringer Dosisleistung sowie die Ergebnisse der Kalibrierung dieses Apparates werden beschrieben. Da die Kammer eine sehr kleine Energieabhängigkeit hat, kann er mit dem gleichen durchschnittlichen Kalibrierungsfaktor für Strahlungsenergien von 40 kV und praktisch bis zur gegenwärtigen oberen Grenze des offiziellen Gültigkeitsbereichs der internationalen Röntgeneinheit benutzt werden.

RÉSUMÉ

L'auteur décrit une chambre condensateur *dosimètre* cylindrique pour la mesure de dose d'exposition pour des radiations à faible débit de dose et donne les résultats de son étallonage. Comme ce dosimètre est très peu dépendant de l'énergie, il *peut* être utilisé avec le même facteur moyen d'étalonnage pour des radiations dont l'énergie va de 40 kV jusqu'à prati-quement la limite supérieure actuelle du domaine officiel de validité de l'unité roentgen internationale.

REFERENCES

1 HULTBERG S, DAHL, O, THORAEUS R VIKTERLOF, K J and WALSTAM, R Kilocurie cobalt 60 therapy at the Radiumhemmet, Chapter III Acta radiol (1959) Suppl No 179
2 RADIOLOGICAL MONITORING METHODS AND INSTRUMENTS NBS Handbook 51 (1952)
3 THORAEUS R A small ionization chamber able to serve as a portable substitute for a standard chamber Acta radiol 22 (1941), 260
4 — Quantitative meaurements of low dose rate roentgen rays in terms of the international r unit by closed ionization chambers Ark Fys 4 (1951) 353
5 — Periodic control of the function and constancy of ionization chamber dosemeters Acta radiol 45 (1956) 503
6 — A substandard condenser dosemeter and its calibration against four national free air standard chambers Acta radiol 48 (1957) 473

ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE NORVEGIAE ET SUECIAE

VOL. 55 MAY 1961 FASC. 5

THE BLOOD VESSELS OF CHONDROSARCOMAS

by

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An investigation by means of microangiographic and histologic techniques has been carried out on malignant mesenchymal tumors in amputated extremities to establish a basis for their angiographic evaluation Previous studies of the vessels in fibrosarcomas and osteogenic sarcomas (Lagergren et coll 1960 1961) have indicated a close agreement between the vascularity and the degree of malignancy There was only slight if any, increased vascularization of the tumor compared with that of the surrounding tissue in cases of low malignancy whereas the great majority of the highly malignant tumors displayed hypervascularization The present article reports a similar study of chondromatous tumors

Angiography was performed in 18 cases of chondromatous tumors of the extremities 16 of these were chondrosarcomas and 2 were chondromas In 5 of the cases of chondrosarcoma and in 2 others in which angiography had not been performed prior to amputation arteriography was carried out on amputation specimens and these were examined in detail by parallel microangiographic and histologic techniques in the manner described in the previous articles

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Submitted for publication 28 October 1960

21 613088 Acta Radiologica Vol 55



Fig 1 Vascular pattern of chondrosarcoma a) Photomicrograph × 35 Tumor lobule surrounded by wide irregular thin walled vessels in interlobular fibrous tissue in places many narrow vessels b) Microangiogram × 7 Lobule for the most part avascular surrounded by a dense network of vessels

Findings

Histology The degree of malignancy in all the tumors was graded according to O NEAL & ACKERMAN in the same way as in an earlier study of chondro sarcomas (LINDBOM, SODERBERG & SPJUT 1961) Out of the 20 tumors examined, 2 were classed as benign chondromas and of the others, which were all chondro sarcomas, 7 were assigned to grade I, 7 to grade II and 4 to grade III In 2 of the tumors that could be examined as a whole, there was a slight difference in the degree of differentiation, with parts of the tumor corresponding to grade I whereas other parts, often peripheral, corresponded to grade II These tumors were, of course, finally graded according to their most malignant parts

The chondromatous tumors had a typical arrangement of vessels, which passed mainly in the connective tissue strands between cartilage lobules (Fig 1a) The higher the malignancy the more numerous and wider the vessels, these often having very thin walls in relation to their width (Fig 2) Two types of vessels were found in the chondrosarcoma, one in which the



a



b



c

F g 2

Photomicrographs × 35 of contrast f lled speci mens howing the ascularity of chond osarcomas of diffe ent degrees of mal gnancy a) grade I b) grade II and c) grade III

\lost of the \ essels contain contrast medium and stand out as dark a eas against the tumor tissue The width number and irregularity of the vessels increase with the degree of malignancy

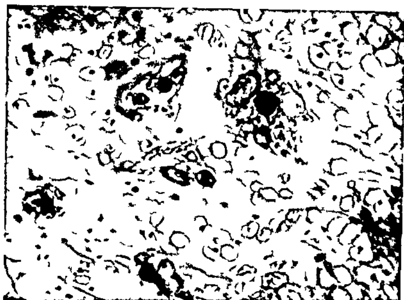


Fig 3 Photomicrograph × 70 of narrow contrast filled vessels (width 10 to 50 microns) penetrating into the peripheral parts of a tumor lobule Chondrosarcoma grade II

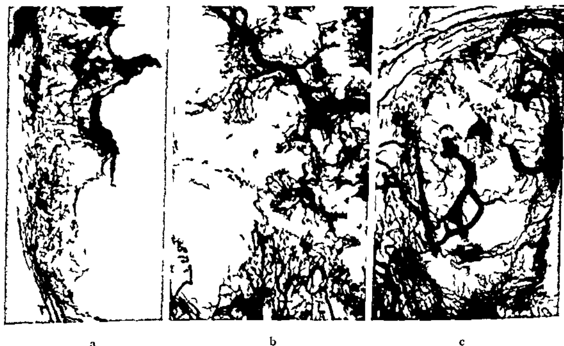


Fig 4 Microangiograms × 10 of chondrosarcomas of different degrees of malignancy a) grade I b) grade II and c) grade III The number and width of the vessels increase with the degree of malignancy The boundary between the neoplastic tissue and the interlobular fibrous tissue containing the vessels is well defined in (a) but increasingly diffuse in (b) and (c) in which large vessels with a brush like ramification are evident

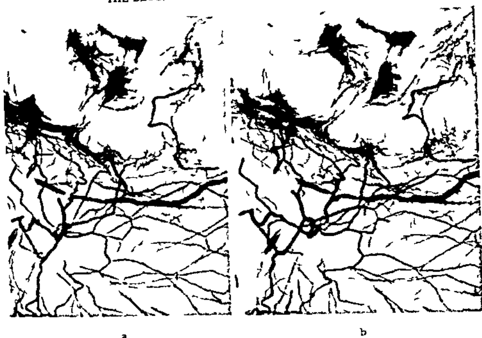


Fig 5 Stereoscopic microangiograms × 10 of chondrosarcoma grade II invading femoral head The vascular pattern of ordinary spongy bone (below) forms a striking contrast to that of the tumor tissue (above) Zone of invasion highly vascular An artery penetrates for a short distance into the tumor tissue (right upper corner)

vessels were wide and sac like, often irregular in shape with very thin walls and 500 to 600 microns in width (Fig 2c), and the other type consisting of small densely packed vessels with a calibre of 10 to 100 microns (Fig 2) These fine vessels were predominantly situated in the connective tissue strands between tumor lobuli but in the less differentiated tumors they showed a tendency to penetrate into the tumor tissue in the peripheral parts of the lobuli with no connective tissue component In the specimens that had been injected with contrast medium, vessels of down to about 10 microns in diameter were observed (Fig 3) However in the actual tumor tissue in the lobuli some lumina contained erythrocytes and Heidenhain staining brought out an arrangement of vessels that suggested that the cells were situated in fine capillaries

Microangiography The typical arrangement of the vessels in the connective tissue strands between the cartilage lobuli gave these tumors characteristic appearances (Figs 1b and 4) The pattern of the vessels was in marked con trast to that of the surrounding tissue (Figs 5 and 6) The often very wide



Fig 6 Roentgenogram of a 0 5 cm decalcified section of contrast filled specimen from a grade III chondrosarcoma of head of humerus *An avascular necrotic part of the tumor surrounded by invading* highly vascular sarcomatous tissue with a scalloped arrangement of vessels lies centrally The tumor stands out clearly by virtue of its hypervascularization

vessels seemed to be flattened out between the lobuli, some were band shaped and their lumina were sometimes triangular in section and often varied in appearance There was, moreover, a characteristic brush like arrangement of the smaller vessels, from the large interlobular vessels there emerged in places a large number of small vessels, 10 to 100 microns in diameter, with comb or brush like arrangements, often running parallel for a short distance into the peripheral zones of the *lobuli* This brush like arrangement of fine vessels was found also in the lower degrees of malignancy but it was considerably more marked in grade III tumors, where they seemed to penetrate more deeply into *the cartilage lobuli The vascularity as evaluated in the microangiograms* bore a distinct relationship to the degree of malignancy assessed histologically (Fig 4)

Angiography Serial films were obtained in most of the angiographic examinations Automatic *filmchangers were used in some cases so that the passage of* the contrast medium through the tumors could be followed more closely Any increase and widening of the arteries supplying the tumors, the presence *of pathologic vessels within the tumors, and shunting of medium through the* tumors were recorded in the angiograms The vascularity of the tumors was graded on the basis of these findings

Comparison was made between the vascularity and the degree of malignancy All the grade III tumors were highly vascular and differed from the rest All the grade I and II tumors were less *highly vascularized than those belonging* to grade III The vascularity of the grade I and II tumors varied widely and



Fig 7 Angiogram in the arterial phase of chondrosarcoma grade III growing in the proximal end of femur with part of the tumor outside the bone Highly vascular tumor tissue with in places a scalloped arrangement of vessels Some veins already contain contrast medium, indicating an arteriovenous shunt through the tumor tissue

no obvious difference between the two classes in this respect could be distinguished in the angiograms In the two chondromas the vascularity was no greater than in the surrounding tissues The interlobular arrangement of the vessels could be observed in some areas in the grade III cases (Fig 7)

Discussion and Conclusions

There was a close agreement between *the* vascularity and the degree of *malignancy* with a high degree of malignancy when vessels were abundant in the chondrosarcomas as in the *fibrosarcomas and osteogenic sarcomas* The chondromatous tumors with a low degree of vascularity were more difficult to evaluate, this group contained *both benign chondromas and chondrosarcomas* of grades I and II It would therefore appear that poor vascularity does not rule out the possibility of malignancy *The presence of more vessels* in a chondromatous tumor than in the surrounding tissues, as seen at angiography, would support a diagnosis of sarcoma *In such cases* any biopsy specimens should be taken from the part of the tumor showing the most marked vascularity

Examination of the vessels in the tumors may prove rewarding in the histologic evaluation of the malignancy of chondrosarcomatous tumors hyper*vascularization* and the presence of pathologic vessels would indicate malignancy

Highly malignant chondrosarcomas provide characteristic microangiographic appearances of wide lumina between the cartilage lobuli, giving a *scalloped contour to the vascular network* fine brush like groups of vessels emerge from the lumina to pass into the peripheral parts of the lobuli The scalloped contour may also be observed in angiograms particularly in parts of a

tumor that can be projected free from other structures The chondrosarcomas of low malignancy are often slow in growth, and in such cases the clinical examination may not suggest malignancy, furthermore, a biopsy specimen may be taken from unrepresentative parts of the tumor and no evidence of malignancy obtained The treatment of such a tumor may in consequence often be insufficiently radical If angiography of a chondromatous tumor reveals highly vascular parts, it should be regarded as malignant and dealt with accordingly

SUMMARY

An investigation of chondrosarcomas by angiographic, microangiographic and histologic techniques is reported The characteristic appearances are discussed and the question of treatment considered Highly vascular tumors were found to be extremely malignant

ZUSAMMENFASSUNG

Eine Untersuchung von Chondrosarkomen mit angiographischer mikroangiographischer und histologischer Technik wird berichtet Das charakteristische Aussehen wird diskutiert und die Behandlung wird besprochen Sehr gefässreiche Tumoren haben sich als ausserordentlich bosartig erwiesen

RÉSUMÉ

Les auteurs présentent une étude des chondrosarcomes par les techniques angiographique microangiographique et histologique Ils examinent leurs aspects caractéristiques et envisagent la question du traitement Les tumeurs tres vasculaires se sont révélées extremement malignes

REFERENCES

LAGERGREN C LINDBOM Å and SODERBERG G Vascularization of fibromatous and fibro sarcomatous tumors *Acta radiol* 53 (1960) 1

— — — The blood vessels of osteogenic sarcomas Acta radiol 55 (1961) 161

LINDBOM Å SODERBERG G and SPJUT H J Primary chondrosarcoma of bone *Acta radiol* 55 (1961) 81

O NEAL L W and ACKERMAN L V Chondrosarcoma of bone Cancer 5 (1952) 551

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MENINGEAL VESSELS OF THE INTERNAL CAROTID ARTERY AND THEIR ANGIOGRAPHIC SIGNIFICANCE

by

STURE STATTIN

The intracranial dura mater is supplied mainly by the middle meningeal artery a branch of the external carotid artery which enters the cranial cavity through the foramen spinosum Other more or less constant branches of the external carotid artery augment the supply These small vessels arise from the superficial temporal artery, the occipital artery the ascending pharyngeal artery and from other branches of the external carotid artery and enter the intracranial cavity through the foramina in the base of the skull through the parietal and condyloid foramina and directly through the calvarium via other small channels Further small and more constant supply vessels are the accessory meningeal artery a branch of the maxillary artery which enters the cranial cavity through the foramen ovale and the posterior meningeal artery which arises from the ascending pharyngeal artery and enters the cranial cavity through the jugular foramen These supply small areas of the dura near the site of entry and freely anastomose with branches of the middle meningeal artery and other meningeal vessels Familiarity with these small meningeal arteries is important because an intracranial tumour supplied by the external carotid artery is almost certainly a meningioma The best method

Based on a paper read at the Meeting of the Swedish Society for Medical Radiology in 1959 Submitted for publication 31 October 1960



Fig 1 Olfactory groove meningioma with vascular supply mainly from a hypertrophic anterior meningeal artery ramifying in the tumour in a broom like fashion



a



b

Fig 2 a) Meningeal branch of the ophthalmic artery supplying a parasagittal meningioma b) Same case Angiography of the external carotid artery

of demonstrating these vessels angiographically is to inject the contrast medium directly into the external carotid artery The introduction of the medium into the common carotid artery will often result in an unsatisfactory filling of the external carotid branches, in addition the origin of tumour vessels may not be determined with certainty if the internal and external carotid arteries are both filled at the same time



Fig 3 Internal carotid angiography in a case of meningioma arising in the anterior part of the middle fossa At operation no vascular supply from the cerebral branches of the carotid artery could be found and the tumour appeared to be supplied exclusively from the dura by the anterior meningeal artery and other meningeal branches of the ophthalmic artery and the carotid siphon

Certain areas of the dura are also supplied by vessels from the internal carotid artery In the anterior fossa the dura draws a part of its blood supply from two branches of the ophthalmic artery namely the anterior meningeal artery and the recurrent meningeal branch of the ophthalmic artery In some cases a meningeal branch, which also supplies the anterior fossa arises directly from the cavernous part of the carotid siphon The anterior meningeal artery usually arises from the anterior ethmoidal artery shortly after this vessel has entered the anterior cerebral fossa through the anterior ethmoidal foramen it supplies a small area of the dura of the cribriform plate The recurrent meningeal branch generally arises from the ophthalmic artery in the optic canal and passing backwards through the lateral part of the superior orbital fissure anastomoses with branches of the middle and anterior meningeal artery The inconstant vessel arising directly from the siphon passes over the lesser wing of the sphenoid and anastomoses with the meningeal vessels mentioned above

These small meningeal vessels especially those of the internal carotid artery have received little attention in the angiographic literature In normal cases they are very narrow and are only occasionally visible at arteriography In cases of intracranial meningiomas they may hypertrophy and the angiographic demonstration of such meningeal vessels points to the correct diagnosis (Figs 1 2 and 3)

The development of the cranial arteries from the primitive branchial arch arteries is very complicated and vessel anomalies in the head and neck are common Descriptions of such anomalies are abundant in the anatomical literature For example the ophthalmic artery or the lacrimal artery may be replaced by branches of the middle meningeal artery Conversely, branches of the ophthalmic artery may take the place of the middle meningeal artery We have seen some cases with this latter type of anomaly The middle meningeal



Fig 1 Olfactory groove meningioma with vascular supply mainly from a hypertrophic anterior meningeal artery ramifying in the tumour in a broom like fashion





a b

Fig 2 a) Meningeal branch of the ophthalmic artery supplying a parasagittal meningioma b) Same case Angiography of the external carotid artery

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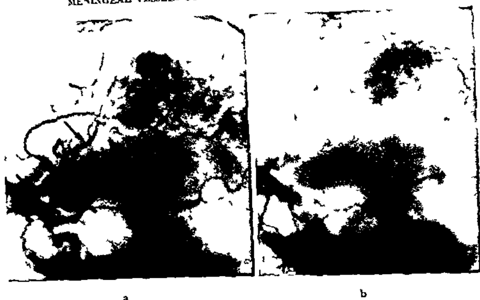


Fig 5 a) Hypertrophic anomalous meningeal vessel arising from the ophthalmic artery and supplying a meningioma at the convexity b) External carotid angiography The anomalous vessel replaces the middle meningeal artery of the external carotid artery which is probably absent

vessel arose from the external carotid artery In one of the cases reported by FRUGONI et coll the vessel did not fill when the external carotid artery was injected separately and considering this fact they had their doubts as to whether the vessel arose from the external carotid artery

We have seen a meningeal vessel that arose from the intracavernous part of the siphon in 8 out of 10 cases of tentorial meningioma examined with internal carotid angiography (Figs 7 and 8) Of the two cases in which the vessel could not be demonstrated the tumour was located in one case far occipitally above the tentorium and in the other case the whole tumour was situated subtentorially We have also observed a similar vessel in 7 additional nonverified cases In one of these the vessel together with branches of the posterior cerebral artery supplied an arteriovenous malformation near the pineal body (Fig 9) In another of the cases the vessel supplied a vascular malformation similar to a cirsoid aneurysm situated in the midline at the anterior attachment of the tentorium In one of the remaining 5 cases the vessel could be traced to the summit of the tentorium, and in the other 4 cases it could be followed towards the free edge of the tentorium Superimposed large cells of the petrous bone made it impossible to determine whether the vessel reached the summit of the tentorium or if it terminated earlier In none of these five cases did any angiomatous vessels fill from the meningeal branch nor could any rapid passage of medium to the veins be demonstrated The angiographic

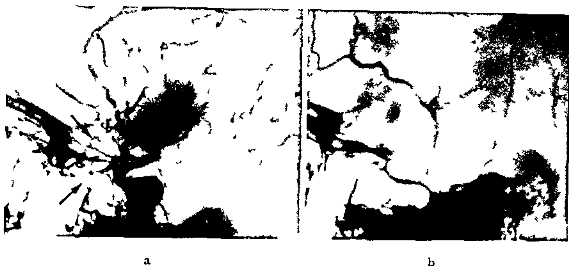


Fig 4 a) Anomalous meningeal vessel branches from the ophthalmic artery The distribution of the vessel is similar to that of the middle meningeal artery b) Same case Injection into the external carotid artery The middle meningeal artery is very narrow

artery which usually arises from the external carotid artery has been small or missing in all these cases, as has the foramen spinosum, and the anomalous meningeal vessel has arisen from the ophthalmic artery (Figs 4 and 5)

In a paper read at the V Symposium Neuroradiologicum (1957) in Bruxelles we described a vessel which arose from the siphon approximately where the internal carotid artery enters the cavernous sinus and, passing backwards to the tentorium, the vessel contributed to the vascular supply of a tentorial meningioma (WICKBOM & STATTIN 1958, Fig 7) In their monograph (1957) KRAYENBUHL and YAŞARGIL illustrate a similar vessel supplying a subtentorial arteriovenous malformation These authors call this vessel the primitive trigeminal artery It is however evident that the vessel is not identical with the persistent primitive connection between the basilar artery and the carotid siphon generally called the primitive trigeminal artery (Fig 6) We have seen this persistent anastomosis in 10 cases, representing 0 2 to 0 3 per cent of our carotid angiographies

BERNASCONI and CASSINARI (1956) noticed in 5 out of 7 angiographies of tentorial meningioma an unusual, narrow artery which they considered to be of specific value in the recognition of such lesions It would appear from the illustrations that the vessel was the same one as described by us FRUGONI et coll (1960) reported 8 cases of tentorial meningioma, 2 cases of meningioma of the falx, and 1 case of parasagittal meningioma in which they demonstrated the same peculiar vessel In both these reports the injection of contrast medium was made into the common carotid artery, and the exact origin of the vessel could not be determined BERNASCONI and CASSINARI suggested that the



Fig 9 A meningeal branch from the siphon supplying an arteriovenous malformation near the pineal body No operation performed b) Same case Vertebral angiography Rapid passage of medium from the malformation (←) to the straight sinus (↔)

the siphon or sometimes crossing the latter The anomalous meningeal artery of the ophthalmic artery mentioned earlier may also appear to come off from the carotid siphon

We have not been able to find any description in the anatomical literature of the meningeal vessel we described In order to find out if the vessel may exist normally we have examined about twenty cadavers some in cooperation with Dr Schnurer at the department of pathology A number of cases were examined with the aid of a special microdissection technique after injection of a water soluble dye into the internal carotid artery and in three of these cases we have found a very narrow vessel arising from the siphon in the region where the internal carotid artery enters the cavernous sinus After passing backwards the vessel ramified in the anterior part of the tentorium anastomosing with other meningeal vessels to this region No such vessel was found in the other cases this might be due to imperfect technique but it might also be that the vessel was missing It seems however reasonable to assume that the vessel may exist normally as an inconstant meningeal branch of the internal carotid artery which in some cases contributes to the vascular supply of the tentorium The chances of seeing this narrow vessel at clinical angiography in normal patients are rather limited Pathologic lesions rich in vessels involving the tentorial region, such as meningiomas of the tentorium and clivus, and arteriovenous malformations in the neighbourhood of the tentorium demanding an increased blood supply may cause this meningeal vessel to hypertrophy which markedly increases the chances of demonstrating it angiographically



Fig 6 Persistent primitive connection between the carotid siphon and the basilar artery generally called the primitive trigeminal artery (arrow)



Fig 7 Meningeal vessel arising from the siphon about where the carotid artery penetrates the outer dura to enter the cavernous sinus It partly supplies a huge tentorial meningioma

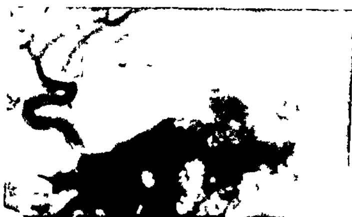


Fig 8 Meningeal vessels from the siphon supplying a tentorial meningioma

diagnoses in three cases were as follows thrombosis of the middle cerebral artery, berry aneurysm of the middle cerebral artery, and complete occlusion of the left and narrowing of the right carotid artery in the neck caused by Buerger's disease, in the latter case there were intracranial vessel anomalies as well The fourth patient suffered from a hissing noise in the ear synchronous with the pulse, and the fifth had a subarachnoidal hemorrhage but no malformation or aneurysm could be seen on internal carotid angiography

The meningeal vessel discussed has in some of the cases been observed only in retrospect The reason probably lies in it having been mistaken for another vessel at the examination In some cases it may be difficult to distinguish it from a branch of the middle cerebral artery passing basally at the level of

FROM THE UNIVERSITY INSTITUTE FOR EXPERIMENTAL MEDICAL RESEARCH (DIRECTOR PROF CARL SEMB) ULLEVAL HOSPITAL OSLO, NORWAY

EXPERIMENTAL ARTERIOVENOUS FISTULAE

by

RAGNAR HOL and RAGNVALD INGEBRIGTSEN

An arteriovenous fistula presents a number of diagnostic, haemodynamic and therapeutic problems The local haemodynamics of experimental femoral arteriovenous fistulae in dogs including the possible diagnostic implications were selected for serial angiographic studies and form the subject of this paper

Vascularization around an arteriovenous fistula has been explored by many authors and is reported to be more abundant than the collaterals which develop following the ligature of a main artery at the same level, the same is true of the progressive arterial dilatation proximal to the fistula

The blood pressure in the proximal part of the artery is always lowered immediately after the opening of an experimental fistula (NEY HOLMAN INGEBRIGTSEN & coll) INGEBRIGTSEN reported a higher blood pressure in the proximal part of the artery than in the artery of the healthy extremity at a corresponding level in two cases and reviewed three other cases from the literature of congenital fistulae of long standing The blood pressure in and around the fistula is evidently of importance as a causal factor in the development of the new vascular pattern The flow to the region is increased and the cardiac output is accordingly augmented facts which are recognised clinically

The direction of flow in the artery distal to larger experimental arteriovenous fistulae was found by HOLMAN (1949) to be retrograde in fistulae in which the length did not exceed that of the arterial diameter the blood flow in the distal

Submitted for publication 19 October 1960

The demonstration of meningeal vessels is of importance in lesions believed to be meningiomas or arteriovenous malformations, since a tumour blood supply from such vessels strongly indicates that the tumour is a meningioma, and a *complete outline of the blood supply of a vessel malformation will be* of considerable value in any operative procedure It must be kept in mind that meningeal vessels arise also from the internal carotid artery Internal *carotid angiography should* be performed, even if a tumour which appears to be a meningioma is situated entirely in the posterior fossa, as our experience which *is supported by that of* TRUGONI *et coll seems to indicate that most* tentorial meningiomas obtain a blood supply from a meningeal vessel arising from the carotid siphon It is our intention to continue our study of the variations in the meningeal vascular supply, especially of those from the internal carotid artery

SUMMARY

The vascular supply of the intracranial dura is discussed with special reference to normal and anomalous meningeal branches of the internal carotid artery A very narrow meningeal artery arising from the siphon and ramifying in the tentorium may exist normally although it will probably be demonstrable at clinical angiography only when hypertrophied and supplying a lesion rich in vessels

ZUSAMMENFASSUNG

Die Gefässversorgung der intrakraniellen Dura wird mit besonderer Bezugnahme auf die normalen und aberranten meningealen Zweige der A carotis interna diskutiert Eine sehr enge meningeale Arterie welche vom Siphon aufsteigt und sich im Tentorium verzweigt kann normal vorkommen *obwohl sie wahrscheinlich bei einer klinischen Angiographie nur* dann nachweisbar sein dürfte wenn sie hypertrophiert ist und eine gefässreiche Erkrankung versorgt

RÉSUMÉ

L auteur a étudié la vascularisation artérielle de la dure mere intracranienne et en particulier les branches méningees normales et anormales de l artère carotide interne *Il* peut exister normalement une très fine artère méningée provenant du siphon et se ramifiant dans la tente du cervelet cependant il ne doit etre possible de la mettre en évidence par angiographie clinique que quand elle est hypertrophiée ou quand elle irrigue une lésion richement vascularisée

REFERENCES

BERNASCONI V and CASSINARI V Un segno carotidografico tipico di meningioma del tentorio Chirurgia 11 (1956) 586

TRUGONI P NORI A GALIGIONI F and GIAMUSSO V A particular angiographic sign in meningiomas of the tentorium The artery of Bernasconi and Cassinari Neurochirurgia 2 (1960) 142

GRAY S ANATOMY 32nd edition Longmans Green & Co London 1958

KRAYENBUHL H und YASARGIL M G *Die vascularen Erkrankungen im Gebiet der Arteria* vertebralis und Arteria basialis Georg Thieme Stuttgart 1957

WICKBOM I and STATTIN S Roentgen examination of intracranial meningiomas Acta radiol *50 (1958) 175*

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artery was in a normal caudad direction. PINOTTI and PUGLIONISI (1955) observed no such retrograde flow in the distal part of the artery in recently established fistulae, measuring 15 to 20 mm in length, although it was present in fistulae of two to three months standing. In femoral arteriovenous fistulae SCHENK et coll. (1957) usually found a 'to and fro' flow in the distal part of the artery although usually directed towards the periphery, with no measurable mean pressure value. HENRIE et coll. (1959) examined the effect of large fistulae in the external iliac vessels and reported venous congestion distal to the fistula with reduction of venous oxygen tension and no signs of venous retrograde flow; they noted reduced arterial flow distal to the fistula and inadequacy of the collateral arterial vessels.

INGEBRIGTSEN & WEHN (1960) studied local blood pressure and direction of flow in experimental femoral fistulae, in those in which the slit was 10 to 19 mm in length retrograde flow was observed in the distal part of the artery and a caudad flow in the distal part of the vein immediately after the establishment of the fistula. The circulatory pattern was unchanged after eight to nine months. In those fistulae in which the length of the slit was about equal to the diameter of the artery, the direction of flow in the vessels distal to the fistula was normal, i. e. caudad in the artery and cephalad in the vein. Blood pressure readings from the distal part of the artery and of the vein always showed much higher values on the arterial side, for instance 200/120 against 40/25, in cases with inverted flow in both channels.

Common to both smaller and larger arteriovenous fistulae is the development of surrounding rich vascularization. The size and pathophysiology of the smaller fistulae are however more like those observed clinically, for instance in traumatic arteriovenous fistulae in human subjects the length of the slit is rarely greater than the diameter of the artery.

Material and technique

Eleven adult mongrel dogs with fistulae between the femoral artery and vein were examined. The fistula was established well above the saphenous vessels by suture with thin vascular silk (Lyon floche) and small straight needles (Kirby 16). Six animals had a large fistula with a slit length ranging from 7 to 19 mm and in one dog bilateral fistulae had been formed. In the remaining five dogs a small fistula had been established, usually with a slit length of about 4 mm, i. e. equal to or less than the diameter of the artery.

In the dogs with large fistulae the examination was performed from 3 days to 25 months after the fistulae were made. The smaller fistulae were examined from the 7th to the 63rd day after their establishment, only one fistula was examined twice.

The augmented flow and the increased vascularization in cases with arteriovenous fistulae allow and necessitate a greater dose of contrast medium than

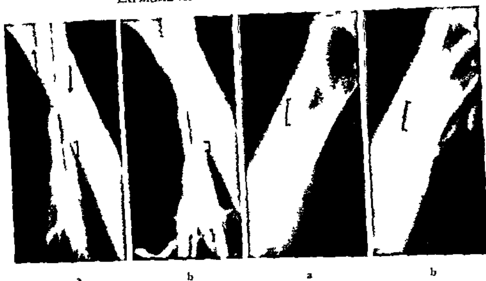


Fig 1 a) Small fistula 9 days after establishment Caudad flow in artery and vein distal to fistula with more contrast medium on venous side Somewhat narrow artery and vein proximal to the fistula, possibly due to oedema b) 54 days later Distal part of artery and vein filled simultaneously and equally the vein is dilated and more conspicuous collaterals have developed Fistula reduced in size proximally a small thrombus Proximal part of vein still of reduced diameter

Fig 2 Large fistula 18 months after establishment 0 25 sec *between (a) and (b)* The distal part of the vein together with the collaterals filled rapidly *The proximal* part of the vein is scantily filled and appears to the right of the artery in this case no narrowing of the vein was observed *The distal part of the* artery was not filled in the first films nor could any reversed flow be observed later

ordinarily given the catheter should be of sufficient diameter and the injections made with a *pressure injection* apparatus A rapid filmchanger is essential to ensure registration of the fistula with the participating vessels before they are masked by the numerous collaterals and varicosities About 1 ml Hypaque 45 % per kg bodyweight was injected through a catheter (size P E 205) introduced percutaneously via the contralateral femoral artery to the lower part of the abdominal aorta *The injection* pressure was 4 5 atmospheres and the first film was obtained at the beginning of the injection The filmchanger was operated at a speed of *four frames* per second for the first ten films the speed then being reduced to two frames per second In the majority of cases this technique proved satisfactory In the animal with bilateral fistulae however an even larger dose and a *more rapid* injection of the contrast medium would have been advantageous As the topography of the fistulae was obvious we had no difficulties in selecting satisfactory projections and films in one plane were deemed sufficient Exposure factors 60 kV 300 mA 0 06 sec 100 cm FFD

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Fig 4 Large fistula 3 days after establishment Distal part of vein is thrombosed close to the fistula The absence of the usual distal venous overflow permits the inverted flow in the distal artery to be observed Appearances are similar to those seen in arterial occlusion except for the leakage towards the fistula.

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The filling of the artery distal to the fistula was very different in cases with small fistulae from that observed in cases in which the fistulae were large The contrast medium in the former cases passed slowly in a caudad direction and in one case intermittent filling occurred, evidently corresponding to the to-and-fro flow reported by SCHENK et coll When the fistulae were large, no primary filling of the distal part of the artery occurred although the popliteal artery was always filled via arterial collaterals In half of the animals of this group direct observation of the region of the fistula in the late phase was masked by numerous tortuous vessels throughout the region The absence of a primary distal artery filling might have been explained by a retrograde flow in these cases in the remaining cases definite late retrograde filling of the distal part of the artery occurred

Arterial and venous collaterals A developed web of collaterals was apparent in all the cases These were developed partly from branches of the femoral artery and vein and partly from the deep femoral and internal iliac vessels The branches from these vessels especially the veins were wider than normal and, by reason of their tortuosity were also elongated The arterial collaterals were filled mainly from arteries proximal to the fistula while the venous collaterals were filled from veins distal to it

A close correlation in time between the filling of the arterial and venous collaterals was regularly observed This correlation was uninfluenced by the



Fig 3 Large fistula 10 days after establishment a) Retrograde filling of the dilated distal part of vein b) Filling of arterial collaterals proximal to fistula and venous collaterals distal to it c) Veins in the whole region together with a widely distributed web of minor arterial collateral branches are well filled The distal part of the artery is filled cephalad via the arterial collaterals proximally the contrast medium is wedge shaped and extends along the whole fistula

Angiographic appearances

The fistula and the participating vessels The demonstration of the fistulae was found to depend on the size of the arteriovenous slit In the cases with smaller fistulae through which the passage was slower and in which the collateral filling occurred later, the fistula was clearly depicted in four to six films, in the cases with larger fistulae and a more rapid circulation through the area, the fistula was observed in one to three films The contrast density was also correlated to the size of the fistula, when the lesion was large the density was reduced However, the site of the fistula was always visible as the starting point of the early venous filling (Figs 1, 2, 3 and 5)

The part of the femoral vein distal to the fistula was more obvious than the other vessels in the period after the contrast medium had reached the fistula In all cases it was dilated, with a caudad direction of flow through incompetent



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a b

Fig 5 Large fistula 25 months after establishment Early filling of single arterial and venous collateral a) Collaterals filled from their respective arterial and venous origins close to the fistula b) Filled intermingled web of collaterals Minute arterial branches proceed distally beyond the web The venous drainage from the area is shown in fig 6a bottom

size and duration of the lesion and by the rate of flow through the fistula There thus appears to be no significant difference in the development patterns of the arterial and venous collaterals The arterial collaterals were less corspicuous than their wider venous counterparts, but were filled with contrast medium earlier than the venous collaterals in the areas proximal to and at the level of the fistula In cases with large fistulae the distal part of the main artery was filled via the collaterals, while in those with small fistulae the arterial collaterals were seen to contribute more or less to the caudad distal arterial flow The venous collaterals distal to the fistula were first observed as they drained the distal part of the femoral vein (Figs 3, 6 7, and 8), the most distal part of the vein had often incompetent valves and hence the venous collaterals drained from a fairly large area

In one case we had the opportunity of observing a single arterial branch with

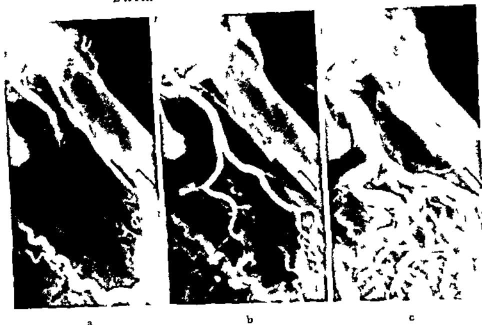


Fig 6 Same case as fig 5 Abundance of collaterals and changing angiographic pattern appearing when the medium has passed the fistula a) Arterial filling proximal to fistula and venous filling distal to it b) Better venous filling but arterial filling still present c) Dominating venous filling but with multiple arterial branches filled distally

collaterals together with the corresponding venous branch to fill with contrast medium before any filling of the other collaterals occurred (Fig 5) The collaterals were filled from their respective arterial and venous origins and in the first film small arterial collaterals were seen to pass from the vascular web more distally in later films other veins were draining the area (Fig 6 bottom)

A further illustration of the development of the collaterals is shown in Fig 7 in which (a) and (b) are from an examination 9 days after the fistula had been established 3 and 5 sec respectively after the commencement of the injection (c) and (d) are from an examination 54 days later 2 75 and 5 sec respectively after the injection Some narrowing of the fistula had occurred between the examinations but despite this the circulation was more rapid in the second examination thus the venous return as shown in (b) occurred after 2 75 sec in the second examination (c) The more distal valves had become competent during the observation time and the venous flow was cephalad in the popliteal region (d) adjacent to the fistula the distal vein had a distal flow as before Together with the free development of venous collaterals the narrowing of the fistula may have contributed to this partial re establishment of normal venous flow

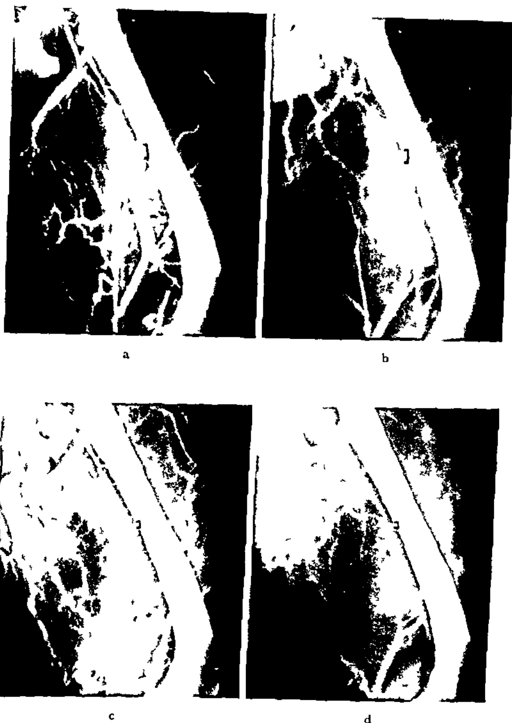


Fig 7 Same case as fig 1 Development of collaterals a) and b) 9 days after establishment of fistula and 3 and 5 sec respectively after start of injection Slow passage of medium distally in the vein through incompetent valves with filling of multiple minor collaterals c) and d) 54 days later and 2 75 and 5 sec respectively after start of injection The collaterals seen in (b) are already filled after 2 75 sec in (c) In the film obtained 5 sec after start of injection (d) the minor venous collaterals have emptied into the larger veins The popliteal vein has now competent valves and is filled from the periphery

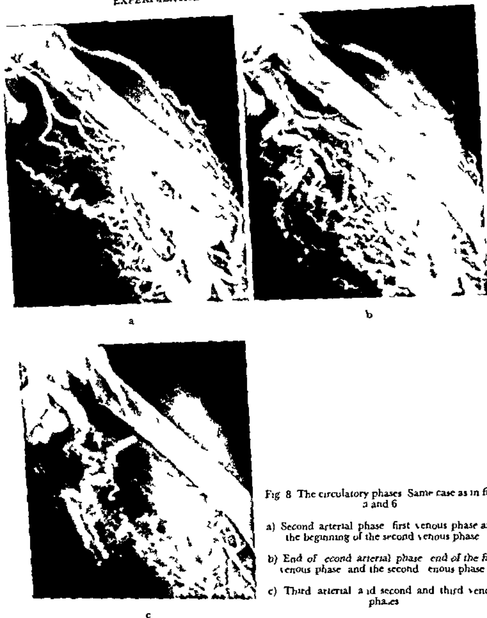


Fig 8 The circulatory phases Same case as in figs 5 and 6

a) Second arterial phase first venous phase and the beginning of the second venous phase

b) *End of second arterial phase end of the first venous phase* and the second venous phase

c) Third arterial and second and third venous phases

The circulatory phases The changing angiographic pattern of a region with an arteriovenous fistula may often be rather confusing As mentioned above the vessels were filled with contrast medium with a more or less unchanged correlation in time as regards *the collaterals* and this was also true for the main vessels with the exception of the distal parts of *the artery*

The following vascular phases, which are shown schematically in Fig. 9, cover the sequence of events in the filling.

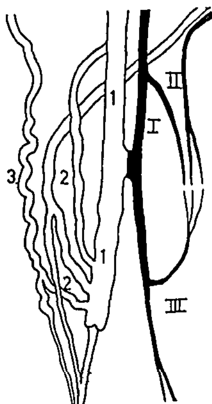


Fig. 9. Schematic drawing of the vascular phases in arteriovenous fistulae. Arterial phases: latin numbers. Venous phases: arabic numbers.

Arterial phases

I. The first arterial phase comprised the rapid filling of the proximal part of the artery and some minor branches arising close to the fistula. A portion of the distal part of the artery was seen filled in cases with small fistulae.

II. In the second arterial phase the contrast medium appeared in the other main arteries to the region (cf. Fig. 8a).

III. The third arterial phase comprised the filling of the arterial collaterals, and in the cases with large fistulae also the filling of the distal part of the artery via the collateral route. In the cases with small fistulae this collateral contribution to the distal arterial flow was not very obvious unless the distal artery flow was slow, or 'to and fro'.

Venous phases

1. In the first venous phase the femoral vein was filled in a distal and proximal direction from the fistula (Figs. 1, 2, 3b, 7a, and 8a). This phase started shortly after the medium had appeared in the proximal artery and ended towards the middle or completion of the second arterial phase.

2. The second venous phase started as soon as some branches from the distal part of the femoral vein were filled with medium, and comprised the venous return through collaterals and the draining to larger proximal veins (Figs. 2b, 3c, 6 and 8). It started slightly later than the second arterial phase and continued into the third arterial phase.

3. The late filling of the very tortuous superficial veins constitutes a third venous phase (Fig. 8c).

Discussion

Angiography in human subjects usually demonstrates numerous collaterals and regional venous overflow in arteriovenous fistulae. The demonstration of the fistula itself may be difficult possibly due to the presence of minute or *multiple* fistulae, or both. Furthermore the vascular topography may be more complex

than in the experimental artificial fistulae between a major artery and vein In the present investigation the technical problems were less when the fistulae were small whereas the importance of rapid injection and film changing was most evident in the larger fistulae A careful observation of the arterial and venous phases might be an aid in finding the correct exposure timing for demonstration of the fistula in clinical cases

Our observations are valid only for communications between a major artery and vein Similar changes will however presumably be found in fistulae between smaller vessels or vessels of different calibre Our investigation would appear to show that apart from the increased flow through the main artery to the region there will also be an augmented flow in the adjacent arteries as judged from the development of arterial collaterals This contribution to the distal part of the artery is more important when the fistula is large The distal arterial flow is then inverted and consequently the collaterals are supplying with arterial blood not only the region distal to the fistula but also the distal part of the main artery with its leakage towards the fistula Thus flowmetric recordings in the proximal part of the artery will not give the total amount of increased load on the circulatory system in arteriovenous fistulae, and the values will be less correct in larger fistulae than in smaller ones

The angiographic findings correspond well with the pressure readings and flowmetric recordings in the cited literature As pointed out by HOLMAN and INGEBRIGTSEN & WEHN the direction of flow in the vessels distal to a femoral arteriovenous fistula depends upon the size of the latter when the length of the slit was larger than the diameter of the artery, we found evidence of inverted arterial flow We never observed a normal flow direction in the distal part of the vein as observed by INGEBRIGTSEN and WEHN in dogs with smaller fistulae Their observation may possibly be explained by difference in the size of the slit in their cases and in the present series of small fistulae In all the present cases the venous valves distal to the fistula were found to be incompetent at least down to the region of the knee in fistulae smaller than those in our experiments the distal venous valves may remain competent In one of our cases a spontaneous reduction in the size of the fistula was observed and in this case some distal valves again became competent

Our constant finding of a reduced size of the vein proximal to the fistula might well be considered as a mechanical attenuation and is in contrast to the observed widening of the vein distal to the fistula This observation corresponds well however to the recording of higher pressure in the distal than in the proximal part of the vein (INGEBRIGTSEN and WEHN) This change in calibre at the site of the fistula might be an aid in localizing the latter in human subjects The site of the fistula may also be evaluated by observing the filling of the arterial and venous collaterals The former are filled from branches proximal to the fistula and the latter from veins distal to it

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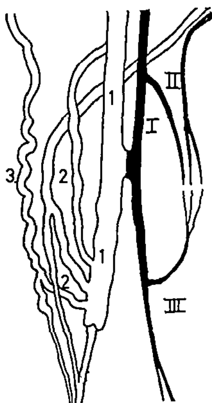


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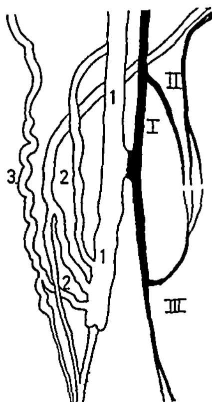


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to the amount of radiation. The number of films in clinical examinations in human subjects must necessarily be greatly reduced although the first 3 to 4 exposures should be made in rapid succession at the beginning of the injection of contrast medium.

The arterial topography of the hind limb in dogs differs from that in man in the case with which arterial collaterals are developed and the manner in which complete ligation of the femoral artery is tolerated. Although the sources for the development of arterial collaterals are more scanty in man, satisfactory vascularization by collaterals may develop following arterial occlusion, and may be far more extensive in cases of arteriovenous fistulae.

Conclusions

Arteriovenous fistulae are better demonstrated when examined with due consideration to the changed haemodynamics, which means with an ample dose contrast medium, rapid injection, and serial roentgenography.

It appears from our series that in cases with a small fistula the distal arterial flow was distad or 'to and fro', and the venous flow distad. In cases with a large fistula both the arterial and venous flow was inverted, i. e. cephalad in the artery and distad in the vein. The vein proximal to the fistula was most often narrowed and the distal part always dilated, with evidence of incompetent valves. The arterial and venous collaterals were developed according to the size and age of the fistula. The arterial collaterals were filled from branches proximal to the fistula and the venous collaterals from veins distal to it.

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SUMMARY

Eleven dogs with experimental large and small femoral arteriovenous fistulae were examined by angiography. The fistula and the participating vessels, the direction of the blood flow, the development of collaterals and the circulatory phases are described. The possibility of localizing fistulae by the shape of the involved vessels, by the origin of the collaterals and by the circulatory phases is considered.

ZUSAMMENFASSUNG

Es wurden 11 Hunde mit grossen und kleinen experimentell erzeugten femoralen arterio-venosen Fisteln angiographisch untersucht. Die Fistel und die beteiligten Gefasse, die Richtung des Blutstromes, die Entwicklung von Kollateralen sowie die Zirkulationsphasen werden beschrieben. Es wird die Moglichkeit der Lokalisierung von Fisteln aus der Form der beteiligten Gefasse, dem Ursprung der Kollateralen und den Zirkulationsphasen besprochen.

RÉSUMÉ

Onze chiens porteurs de grosses et de petites fistules artério-veineuses fémorales expérimentales ont été examinés par angiographie Les auteurs décrivent la fistule et les vaisseaux qui y participent, la direction du courant sanguin le développement des collatérales et les phases circulatoires Ils examinent la possibilité de localiser des fistules d apres la forme des vaisseaux interessés d apres l origine des collatérales et d apres les phases circulatoires

REFERENCES

HENRIE J N JOHNSON E W WAKIM K G and ORVIS A L The influence of experimental arteriovenous fistula on the healing of fractures and on the blood flow distal to the fistula Surg Gynec Obstet 108 (1959) 591

HOLMAN F *Problems in the dynamics of blood flow Surgery 26 (1949) 889*

— and TAYLOR C Problems of dynamics of blood flow pressure relations at site of arteriovenous fistula Angiology 3 (1952) 417

INGEBRIGTSEN R Local blood pressure in relation to congenital arteriovenous fistula of the extremities Acta chir scand 118 (1959) 86

— and WEHN P Local blood pressure and dire tion of flow in experimental arterio-venous fistula Acta chir scand 120 (1960) 142

— JOHANSEN K MULLER, O and WEHN P Blood pressure of the proximal artery in experimental arterio-venous fistulas of long standing Acta chir scand Suppl 253 (1960) p 134

NEY E Über die Bedeutung der Venen bei a v Aneurysmen Arch klin Chir 100 (1912—13) 531

PINOTTI O PUGLIONISI A e BRUNO F *Modificazioni emodinamiche nei vasi affluenti ed* effluenti di anastomosi artero-venose femorale chroniche sperimentali Boll Soc ital Biol sper 32 (1956) 417

— — — *Direzione e velocita del flusso sanguino nell* arteria distale di fistole artero-venose femorale sperimentali acute e chroniche Boll Soc ital Biol sper 32 (1956) 419

SCHENK JR W G BAHN R A CORDELL A R and STEPHENS J G The regional hemodynamics of experimental acute arterio-venous fistulas Surg Gynec Obstet 105 (1957) 733

— MARTIN J W LESLIE M B and PORTIN B A The regional hemodynamics of chronic arterio-venous fistulas Surg Gynec Obstet 110 (1960) 44

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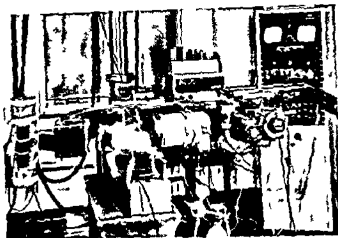


Fig 1 Cat with microphone on chest is inside the C mount which supports the roentgen tube and the Philips image intensifier The high speed camera is in apposition to the lens of the image intensifier while its side lens is viewing the oscilloscopic screen on the table behind the C mount

McDONALD (7) used high speed cinematography to study aortic blood flow by direct transillumination of the artery Prior to the development of image intensifiers an impractical high capacity generator with rapid high tension switching would have been required even for experimental animals for direct cinefluorography of the conventional screen at high speeds (250 frames/second) Since image intensifiers increase the brightness of the fluoroscopic screen 500 to 1 500 times conventional roentgen generators may be used for high speed cinefluorography The camera used in this study has the advantage of a side lens for taking simultaneous oscillo copic tracings on the same film, allowing precise timing of the fluoroscopic events

Flow patterns within the cavae of intact animals have been studied with the above technique (Fig 1) Since minimal surgery is required, there is little alteration in the normal physiology of these animals It is the purpose of this paper to elaborate on this technique and to indicate its experimental application

Image intensifier A 5 inch Philips image intensifier equipped with an f/1 5 to 50 mm lens mounted at its focal distance from the output phosphor, was used The emergent rays were thus approximately parallel The camera lens focused at infinity was brought into apposition with the lens of the image intensifier A right angle viewer with a partially reflecting pellicle was used for monocular viewing while the cine studies were being obtained This resulted in a loss of approximately six per cent of the light passing from the image intensifier to the camera (9)

FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR PROF H M STAUFFER), THE DEPARTMENT OF PHYSIOLOGY (DIRECTOR PROF M J OPPENHEIMER), AND THE DEPARTMENT OF MEDICAL PHYSICS (DIRECTOR PROF G C HENNY) OF THE TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA, PENNSYLVANIA, U S A

FLOW PATTERN ANALYSIS OF PARTICULATE CONTRAST MATERIAL IN BLOOD VESSELS

Experimental cinefluorography at 260 frames/sec, superimposed oscillography of cardiovascular events, and automatic data reduction

by

JOSE L GIMENEZ, BARBARA L CARTER, GEORGE H STEWART and PETER R LYNCH

More precise and detailed analysis of vascular flow patterns is now possible with newer developments in cinefluorographic techniques Previously BOEHME (1) and RUSHMER (9) used cinefluorography to study venae cavae flow patterns but were limited by the relatively slow camera speeds Extensive studies were also done on the same problem by BRECHER (2, 3) using a bristle flow meter, however this technique required considerable surgery BOEHME and BRECHER stated that the dominant blood flow occurred in the cavae during ventricular systole The latter author also noted as mentioned earlier by BURTON OPITZ (4), that the systolic flow became less dominant as the heart rate changed from tachycardia to bradycardia The results of RUSHMER were contradictory to those of BOEHME and BRECHER so that further study in this area seemed indicated

Submitted for publication 29 August 1960

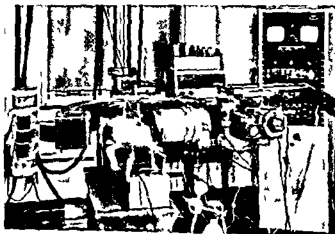


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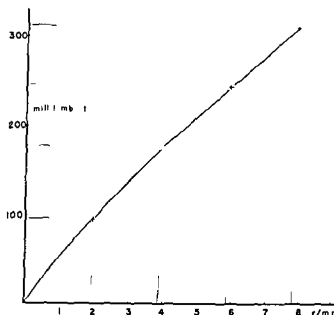


Fig 2 Brightness of output phosphor versus r/min at intensifier

The brightness of the output phosphor of this image intensifier was found to be directly proportional to the roentgen at the input screen for a constant kilovoltage (Fig 2) Using a constant r/min at the surface of the image intensifier, the effect of kilovoltage on the brightness of the output phosphor was evaluated As shown in the Table below, the intensifier was found to be slightly more efficient with higher kilovoltage No phantom was used in any of these determinations An RCA microammeter, used to measure the photocathode current of the image intensifier, served as a brightness control of the output phosphor

The high speed camera The Kodak Industrial High Speed Camera is designed for making variable speed motion pictures up to 3 200 frames per second It was modified to operate reliably at 260 frames per second for this particular project (The camera was made available and specially modified for this

Table

Effect of kilovoltage on brightness of output phosphor of image intensifier

kVp	HVL in mm Al	Millilamberts for 1 r/min at the intensifier surface
60	1 9	44 9
70	2 0	48 6
80	2 2	51 0
90	2 5	51 7
100	2 7	52 4

Fig 3 Diagrammatic sketch of the optical arrangement (Courtesy by Eastman Kodak Co)

application through the courtesy of Eastman Kodak Company, Rochester N Y) The camera is driven by a synchronous motor which operates on 115 volt alternating current It is equipped with a lamp which flashes time makers along one edge of the film at intervals of 8 3 milliseconds The camera has two optical systems at right angles The front lens (Kodak Cine Ektar 25 mm f/1 9) was used for the fluoroscopic image which in turn was refracted through a plane parallel glass of precise thickness rotating behind the lens as the film traveled downward The image thus followed the film and was held on it long enough to expose the emulsion Simultaneous recordings of oscilloscopic tracings were made on this same film through the side lens (Kodak Cine Ektar 63 mm f/2) (Fig 3)

A Tektronix type 502 dual beam oscilloscope with a P 11 phosphor was used Various parameters such as the blood pressure heart sounds ECG and respiration were thus recorded

Eastman Tri X Reversal 16 mm film was used and was processed as a negative film with the Automatic Minirapid Processor (Fairchild Camera and Instrument Company Syosset, New York) using double strength roentgen ray solutions This unit permits loading in daylight and does not require the use of a leader A temperature of 80 F with a processing speed of 1 to 1/2 feet per minute was used.

The roentgen source Four valve full wave rectification was used In order to minimize the ripple at high intensities a high voltage condenser of 0 25 micro farads was installed in series with the transformer The resultant variation in density of the movie films was small enough so as not to be disturbing when the

film was projected in motion The factors used varied from 75 to 110 kV, 3 to 25 mA, with a target screen distance of 30 inches

An additional protective device was designed because of the occasional high roentgen exposure It consisted of a lead covered work table and a frame supporting overlapping lead strips which surrounded the animal With the cage in place over a phantom, the following readings were obtained

kVp	Milli ampères	Position of ionization chamber	mr per hour
80	10	Observer at image intensifier site	6
80	10	25 cm below intensifier	2 5
80	10	Position of operator adjusting oscilloscope	0 4
80	10	Position of hands of operator at roentgen tube side (injection)	40

A comparative measurement with the ionization chamber 52 cm lateral to the field yielded the following results 50 mr per hour with no phantom in place, 160 mr per hour with phantom in place, 26 mr per hour with protective frame placed over the phantom

Data reduction from film The films were projected with a Kodak Analyst at 16 frames per second for a general survey of the dynamic events Frame by frame analysis was then done with a Vanguard Motion Analyzer (Vanguard Instrument Corporation, Roosevelt, New York), a model which provided precise ten diameter magnification of the movie film projected on a ground glass screen (Fig 4) This analyzer is equipped with adjustable hair line X and Y coordinates superimposed on the projected image and a frame counter The projection head can be rotated 360° to align angular motions on the projected image with either of the coordinates Data can be extracted directly from the device or converted to electrical digital form by means of commercially available analog to digital converters or 'digitizers' Once in digital form the data can be recorded on punch cards, magnetic tape or any other form desired for further processing

For this particular project the Vanguard Analyzer has been modified in several ways to facilitate the reduction of data Electric analog readout of the Y coordinate and frame count has been added This permits the direct plotting of one axis of displacement versus film frames or time on a standard electronic X—Y plotter To provide Y axis analog readout, a 40 turn potentiometer has been coupled to the Y axis cursor drive through anti backlash gearing Suitable scale factor and zero adjustments as well as a mercury battery supply have been included To provide the time analog signal, a 40 turn potentiometer is directly coupled to a stepping motor which is driven synchronously with the film advance motor Thus with each film frame advance the motor and potentiometer move ahead one step Suitable scale factor, zero adjustment and mercury battery power have been provided

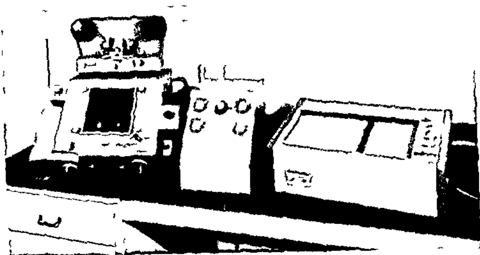


Fig 4 Eq pment for analys of f m Left to right Vanguard Motion Analy er control panel and X—Y Varplotter

Since some motions were relatively slow analysis of every frame was un necessary and systematic sampling proved adequate To facilitate this procedure the Vanguard film advance circuit was modified to automatically move the film a certain number of frames An advance of 1 2 3 4 6, 8 12 or 24 frames can be selected on a front panel switch Additional modifications were incor porated to make a dot on the graph by momentarily dropping the pen on the X—Y plotter This sequence of events wa initiated by a push button on the analyzer

The net result of the modification was to enable a single operator to quickly reduce the film data to a series of dots on the graph paper which are a plot of single axis displacement versus time (Fig 5) Once in this form, the data can be additionally processed to obtain the velocity and acceleration of the mo tion For this the X—Y plotter becomes a function generator An accessory unit will automatically follow a properly prepared curve giving an electrical analog of displacement versus time This signal may be singly or doubly dif ferentiated by a simple computer circuit to give the velocity or acceleration of the motion This must be plotted on a second X—Y plotter

Accuracy of the system The basic accuracy of this data system must be con sidered in several parts One is the inherent error of the equipment in analyzing displacement of droplets vs time A lead rule milled precisely at one centi meter intervals was placed in the same location as the animal and cineradio graphic recordings were obtained These centimeter intervals were then re duced to a eries of dots on graphic paper using the Vanguard projector and

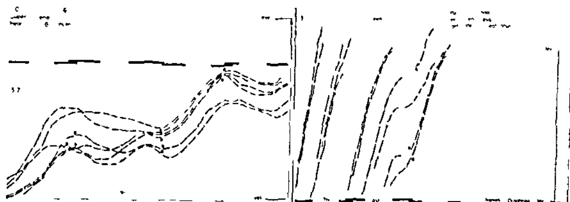


Fig 5 (a) Superior vena cava tracings as recorded through the X—Y Variplotter 1 mm on Vanguard screen equals 1 59 mm at mid sagittal plane of experimental animal 1 frame equals 3 84 milliseconds (b) Inferior vena cava tracings as recorded through the X—Y Variplotter Conversion factors same as in (a)

the Variplotter Four investigators each made five sets of curves to determine individual discrepancies and variation from one person to another With this approach, all static system errors from the roentgen source to the graph paper were included The total error was found to be too small to evaluate quantitatively Errors due to roentgen ray geometry (variation in magnification) and resolution were also minimal, though of greater magnitude than that of the system itself The accuracy of the time coordinate when using power line frequency as the standard had very little error

A second consideration is the method of recording the droplet movement Studies of motion blurring and of light persistence with image intensifiers have shown that the initial rate of decrease in light intensity is so rapid that the phosphor 'lag' does not interfere with the usefulness of photographic exposures of two milliseconds or less per frame in 'stopping rapid motion with high speed cinefluorography Motion unsharpness due to the frame rate of the camera has been evaluated by photographing a rotating disc (10) Blurring was found to be negligible at the rate of 260 frames per second and with linear velocities up to 120 cm/second

The third consideration is related to the determination of velocity, the slope of the curve recorded on the Variplotter A special protractor was calibrated for reading the velocity in cm/sec directly from the slope of the curve The accuracy depends on the ability of the operator to match this protractor with the curve The error in per cent of reading is given by the expression

$$\%\ \text{error} = \left[\frac{\tan(\alpha \pm \Delta)}{\tan \alpha} - 1\right] \times 100$$

Δ = error in reading true angle (degrees)

α = true angle

The error is small for slopes of less than one but as the slope increases above one the error increases rapidly By appropriate choice of scale factors, the lope can be reduced to minimize this error

Experimental application

FRANKLIN and JANKER (5) BOEHME (1) and RUSHMER (9) have used cine fluorography to study flow patterns of contrast material within the venae cavae of intact animals The equipment described in this paper allows a more complete and concise analysis of these flow patterns The movement of particulate contrast material in the inferior and superior vena cava was recorded by the high speed movie camera with simultaneous cardiac parameters from the oscilloscope Subsequent frame by frame analysis was used to correlate caval flow pattern with various cardiac events Lipiodol and ethiodol droplets, the majority measuring 2 mm in diameter or CO_2 bubbles (8) were used as con trast material The movement of these small droplets gave an indication of blood flow in the vessels The range of the velocities was 4 to 60 cm/sec

Comparisons in flow pattern between bradycardia and tachycardia have been studied in cats and dogs It was found that the droplets in the superior vena cava moved 2 to 3 times slower than those in the inferior vena ca a As has been shown in previous investigations a difference was noted between tachycardia and bradycardia in the superior vena cava with tachycardia the droplets moved forward during systole but stopped or moved retrograde during diastole (Fig 5a) These studies have shown a different flow pattern in the inferior vena cava (Fig 5b) the droplets moving forward both during systole and diastole The difference between the two cavae was not as apparent with bradycardia, both showed forward movement with systole and diastole A detailed presentation of these physiologic studies appears elsewhere (6)

Acknowledgements

The following grants from the National Heart Institute U S Public Health Service in support of this work are gratefully acknowledged Research Grant H-4702 post-doctoral training grant, HTS-5362 (for J L. ( ) and post-doctoral fellowship research grant HF-8287 (for B L C)

SUMMARY

High speed cinefluorography at 260 frames per second with simultaneous oscilloscopic tracings has been used in the study of caval flow patterns in animals The equipment and the method for concise analysis of film records including automatic data reduction are described Analysis of droplet movement has revealed a difference in the flow pattern between the superior and inferior venae cavae during tachycardia and bradycardia.

ZUSAMMENFASSUNG

Kinefluorographie mit 260 Bildern pro Sek mit gleichzeitiger oscillographischer Kontrolle ist beim Studium des Blutflusses in der V cava bei Tieren benutzt worden Die Ausrustung sowie die Methode fur genaue Analyse der Filmstreifen einschliesslich automatischer Data reduktion werden beschrieben Die Analyse von Tropfchenbewegungen hat einen Unterschied im Blutfluss zwischen der V cava superior und der V cava inferior wahrend einer Tachykardie und einer Bradykardie aufgezeigt

RÉSUMÉ

Les auteurs ont utilisé la cineradiographie rapide a 260 images par seconde avec enregistrements oscillographiques simultanés pour étudier la circulation cave sur des animaux Ils decrivent l appareillage et la méthode d analyse des enregistrements sur film avec réduction automatique des données L analyse du mouvement de gouttelettes a montré une différence de type de débit circulatoire entre les veines caves superieure et inferieure au cours de la tachycardie et de la bradycardie

BIBLIOGRAPHY

1 Boehme W The active role of the heart in the propulsion of venous blood Ergebn Physiol 38 (1936) 251

2 Brecher G A Venous return Grune and Stratton New York 1956

3 — Cardiac variations in venous return studied with a new bristle flowmeter Amer J Physiol 176 (1954) 423

4 Burton Opitz R The flow of the blood in the external jugular vein Amer J Physiol 7 (1902) 435

5 Franklin K J and Janker R Effects of respiration upon the venae cavae of certain mammals as studied by means of X ray cinematography Amer J Physiol 81 (1934) 434

6 Lynch P R Carter B L Gimenez J L and Krisch R Venae cavae flow pattern in cats as studied with high speed cinefluorographic technique Amer J Physiol 199 (1960) 1139

7 McDonald D A The velocity of blood flow in the rabbit aorta studied with high speed cinematography J Physiol 118 (1952) 328

8 Oppenheimer M J Durant T M Stauffer H M et coll In vivo visualization of intracardial structures with gaseous carbon dioxide Amer J Physiol 186 (1956) 325

9 Rushmer R Cardiac diagnosis a physiologic approach W B Saunders Co Philadelphia 1955

10 Stauffer H M Oppenheimer M J Soloff L A and Stewart G H Cardiac physiology revealed by the roentgen ray Amer J Roentgenol 78 (1957) 195

11 — — Stewart G H and Lynch P R Cinefluorography by image amplifier techniques J appl Physiol 8 (1955) 343

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR PROF KNUT LINDBLOM), KAROLINSKA SJUKHUSET, STOCKHOLM SWEDEN

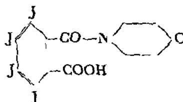
EXCRETION IN THE BILE AND URINE OF A BILIARY TRACT CONTRAST MEDIUM

An experimental study in the rabbit

by

JAAN NOVEK

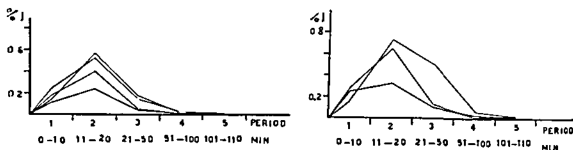
Of a series of iodized compounds prepared by SKAGIUS & EKEMARK the N methyl glucamine salt of 3 4 5 6 *tetra iodophthalic* acid morpholide (Ph 761/3 *see formula below*) showed very promising properties as a roentgen



Formula of 3 4 5 6 tetra iodophthalic acid morpholide

contrast medium The gallbladder filled rapidly when the medium was *given* intravenously in preliminary tests in the rabbit *Since its* acute toxicity in earlier experiments had appeared to be low (2 g/kg *mice*) the compound was selected for further study A closer investigation of the toxicity of the substance (EDLUND & ZETTERGREN) have however made it clear that the compound is not suitable for clinical use

Submitted for publication 19 September 1960



Diagrams 1 and 2 Iodine concentration in the choledochal bile after doses of Ph 761/3 of respectively 0 06 and 0 11 g/kg bodyweight

The excretion in the bile and urine of the contrast medium was studied in the rabbit and the results are now presented An earlier series of experiments with Biligrafin in the rabbit (NOVEK 1959) served as control material

Technique The rabbits were not deprived of food or water Laparotomy and duodenotomy were performed under mebumal anaesthesia and a polythene tube (No Pe 160) 17 cm in length was introduced into the common bile duct the cystic duct was not ligated In the males the urinary bladder was emptied by catheterization just before the start of the experiment In the females, the bladder was not emptied by aspiration until the end of the experiment in this group then, the urine collected was composed of the amount present before the commencement of the experiment as well as that produced during its course At the conclusion of the experiment the gallbladder was excised and the gross appearances of the liver and kidneys were noted Only healthy animals are included in the report

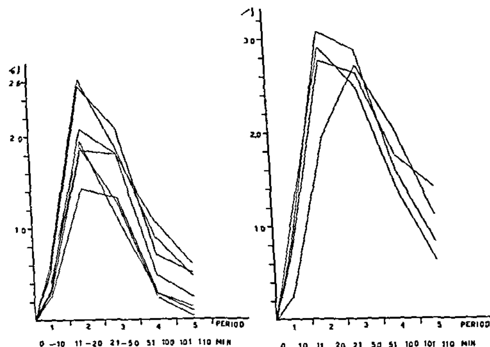
The bile flow during the 10 minutes preceding the injection of the contrast medium was taken as a control sample When the injections had been completed the bile was collected during the following standard periods 0—10 11—20 21—50 51—100 and 101—110 minutes

The experimental animals comprised 18 rabbits Four of them were given 0 06 g/kg three 0 11 g/kg seven 0 32 g/kg and four 0 56 g/kg bodyweight Ph 761/3

Results

The concentration of iodine in the bile was analysed after injection of the different doses of Ph 761/3 (Diagrams 1 to 4) A dose of 0 06 g/kg bodyweight gave the highest iodine concentration of between 0 24 and 0 57 per cent, after a dose of 0 11 g/kg the highest concentration of iodine ranged from 0 33 to 0 73 per cent The maximum values obtained with a dose of 0 32 g/kg body weight lay between 1 43 and 2 62 per cent, and with 0 56 g/kg between 2 70 and 3 06 per cent iodine With one exception the highest iodine concentration was recorded in the 11—20 min period In the exception the peak value was not recorded until the 21—50 min period, the bile flow during the first interval in this instance was appreciably lower than in the other experiments in this series

Initially Ph 761/3 always reduced the bile flow The fall was noted promptly after the injection of the contrast medium and amounted on the average to



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between 50 and 70 per cent, although the individual variations were wide The reduction in flow was not related to the size of the dose The initial decrease was in some instances followed by a temporary slight increase in flow This increase was not accompanied by any reduction in the iodine concentration thus the admixture of gallbladder bile was unlikely

The percentage excretion as measured in the common duct was fairly uniform and ranged from 12 to 24 per cent after doses of 0 06 and 0 11 g/kg bodyweight The excretion also varied little after doses of 0 32 and 0 56 g/kg bodyweight and ranged from 21 to 34 per cent

The contents of the gallbladder were examined in 9 cases A dose of 0 11 g/kg for instance gave a concentration of between 0 10 and 0 40 per cent iodine while an iodine concentration of between 1 35 and 2 64 per cent was recorded after a dose of 0 56 g/kg body weight The iodine concentration in the gallbladder was as a rule higher than the mean iodine concentration in the choledochal bile within 110 minutes At the conclusion of the experiment between 0 08 and 3 85 per cent of the contrast medium injected was recovered from the gallbladder

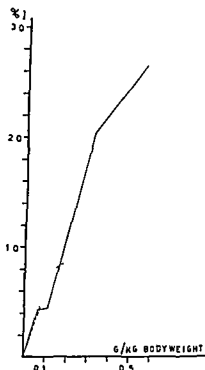


Diagram 5 The mean maximum iodine concentration after different doses of Ph 761/3 ( ) and Biligrafin ( )

The excretion in the urine was examined in 12 cases In two instances the urinary volume was fractionated This showed the iodine concentration to reach its highest values in the latter half of the experiment The percentage excretion following doses of 0 06 and 0 11 g/kg varied between 30 and 65 per cent, and after doses of 0 32 and 0 56 g/kg bodyweight between 13 and 49 per cent

Discussion and Conclusions

The mean maximum iodine concentration in the choledochal bile was 0 43 per cent after a dose of 0 06 g/kg and 0 57 per cent after a dose of 0 11 g/kg bodyweight A dose of 0 32 g/kg gave an iodine concentration of 2 05 per cent, and one of 0 56 g/kg gave 2 67 per cent iodine The iodine concentration in the choledochal bile was thus greatly dependent upon the size of the dose Doses of both 0 06 g/kg and 0 11 g/kg of Ph 761/3 gave lower iodine concentrations in the choledochal bile than 0 12 g/kg of Biligrafin However, the highest dosage of Ph 761/3 gave up to twice the iodine concentration produced by Biligrafin (Diagram 5) Further, a dose of approximately 0 15 g/kg of Ph 761/3 was estimated to give an iodine concentration equal to that of a similar dose of Biligrafin

The highest iodine concentration following the administration of Ph 761/3 was regularly recorded in the 11—20 min period With Biligrafin, the highest values were noted in different intervals depending upon the dosage

The percentage excretion in the bile of Ph 761/3 differed from that of Biligrafin Increasing doses of Ph 761/3 led to an increasing excretion of the medium while with Biligrafin the excretion diminished, even large doses of Ph 761/3 never led to excretion so high as that following small doses of Biligrafin

The total excretion in the bile and urine of Ph 761/3 within a period of 110 minutes was good and ranged from 40 to 80 per cent

Acknowledgement

The author would like to thank Mr Kurt Skagius Ph D of AB Pharmacia Uppsala for his valuable advice and help in compiling the analytical data The author is also indebted to this firm for the financial aid and iodine analyses which made the study possible

SUMMARY

The excretion in the bile and urine of an experimental biliary tract intravenous contrast medium was studied in healthy rabbits under mebumal anaesthesia This medium gave iodine concentrations in the choledochal bile that were up to twice those given by Biligrafin and the total excretion was good

ZUSAMMENFASSUNG

Die Ausscheidung eines experimentellen intravenosen Mittels fur das Gallengebiet in die Galle und in den Urin wurde an gesunden Kaninchen in Mebumalnarkose studiert Dieses Mittel gab eine Jodkonzentration in den Gallengangen die bis zu zweimal grosser war als die welche man mit Biligraphin erhalt und die totale Ausscheidung war gut

RÉSUMÉ

L auteur a étudié chez des lapins sains sous anesthésie au mebumal l excrétion biliaire et urinaire d un moyen de contraste biliaire expérimental administré par voie intraveineuse Ce moyen de contraste a donné dans la bile cholédocienne des concentrations d iode s élevant jusqu au double de celles données par le Biligrafin et l excrétion totale a été bonne

REFERENCES

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SKAGIUS K and EKEMARK A Personal communication

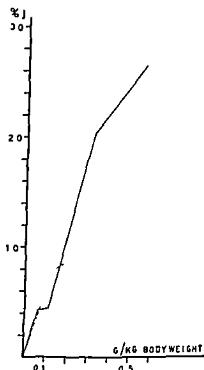


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SKAGIUS K and EKEMARK A Personal communication

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF GREGERS THOMSEN), RIGSHOSPITALET (UNIVERSITY HOSPITAL), COPENHAGEN, DENMARK

DISSECTION OF THE AORTIC WALL IN RETROGRADE LUMBAR AORTOGRAPHY

by

C L GUDBJERG and JAN CHRISTENSEN

Injury to the arterial wall with subsequent intramural deposition of contrast medium is now a well known complication of direct percutaneous lumbar aortography and was first reported by GAYLIS & LAWS in 1956 In a comprehensive review of 13 207 lumbar aortographies from 301 clinics in U S A the incidence of this complication was reported to vary from 1 to 20 per cent The available literature appears, however, to contain no collected survey on the incidence of intimal injury caused by percutaneous retrograde aortography using the catheter technique of SELDINGER with insertion of the catheter via the femoral artery We therefore reviewed all abdominal aortographies performed in our department during the period 1953—1959 with a view to assessing the frequency of this type of injury The material comprised 451 investigations The distribution according to technique, and indication, with the incidence of intimal damage, in brackets, was as indicated below

Technique	Indication	Number of cases
Retrograde	Arteriosclerosis	126 (36)
	Other diseases	293 (0)
Direct	Arteriosclerosis	31 (6)
	Other diseases	1 (0)
	Totals	451 (42)

Submitted for publication 11 October 1960



Fig 1 a) 2 sec after injection of contrast medium Arcuate filling defect in the distal part of the aorta b) 10 sec later A deposit of contrast medium still remains in the vascular wall

The injuries occurred only in patients examined for probable circulatory disturbances in the lower limbs due to arteriosclerosis

The aortographic appearances of an intimal injury generally consist of a sharply defined arcuate filling defect with a subintimal deposition of contrast medium the latter being an almost constant finding in all the films The deposit was found in most of the cases to have persisted after the remainder of the contrast medium had left the blood stream (Fig 1) Less commonly and when the injury is marked the intramural contrast medium may be spread around the circumference of the vessel for a varying distance (Fig 2) this was particularly evident in a few cases in which contrast medium was present below large areas of the intima (Figs 3 and 4) A characteristic finding in these cases also was that the appearance throughout the film was constant and unchanged

Discussion and Conclusion

We demonstrated signs of an intramural deposition of contrast medium in 36 out of 419 aortographies This corresponds to an incidence of 9 % exactly the same as that reported in direct lumbar aortography (Boblitt Figley & Wolfman 1959 McAfee 1957)

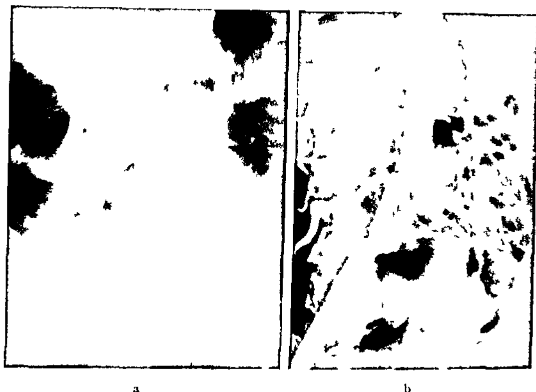


Fig. 2. a) Tubular deposition of contrast medium beneath the intima simulating total obstruction. Appearances unchanged in all the films of the series. No collaterals present. b) 2 days later same technique. *No occlusion of the aorta but thrombosis at the level of the origin of the left common iliac artery.*

However, it is important to remember that all the complications in our series occurred in patients with preexisting clinical signs of arterial wall abnormalities. When calculated on the basis of this group of patients alone, the incidence is no less than 29 %. This supports our view regarding the pathogenesis of this injury, viz. that the catheter is caught by an arteriosclerotic plaque, passes beneath it, and then proceeds below the intima for a shorter or longer distance, the injury always occurs in the region of the tip of the catheter from which a major or minor intramural spread of contrast medium is evident. This assumption receives further support from the fact that in 27 out of the 36 cases of damage, there had been difficulties in inserting the catheter (slight resistance to the insertion or inability to pass the catheter to the desired level). That the injection was nevertheless performed appears to have been due to the occurrence of a free reflux of blood from the catheter prior to the injection of the contrast medium and to the contralateral femoral artery not being accessible to puncture.

All the investigations were carried out by the same slightly modified Seldinger technique. The number of intimal injuries was evenly distributed among four different examiners.



F g 3 Extens ve tubular intramural deposit on of contrast medium in the aorta and il ac a te es



Fig 4 Marked injury with subint mal spread of contrast medium from the aorta to the fe moral artery

No clinical signs in association with the infliction of the injuries were ob served but 7 patients complained of slight pain 4 of these still had slight low back pain the next day The damage should however not be neglected since it may contribute to the development of dissecting aneurysm (BOBLITT et coll McAFEE)

The deposition of contrast medium beneath the intima may give rise to errors in diagnosis This applies in particular to cases in which the medium spreads in a tubular fashion beneath large areas of the intima, since this may simulate obstruction due to thrombosis

Summing up it may be said that intimal injury is not particularly un common but probably involves a risk of untoward sequelae In the event of resistance to the catheter insertion, therefore the injection should be per formed later or else carried out by the direct percutaneous route

SUMMARY

The authors report the incidence of intimal injury followed by deposition of contrast medium in the vascular wall in 29 % of cases in a series of 419 retrograde percutaneous abdominal aortographies This complication was confined to cases of arteriosclerosis and did not occur in other cond tions

ZUSAMMENFASSUNG

Die Autoren berichten uber das Vorkommen von Intimaschaden als Folge von Kontrast mittelinjektion in die Gefass and Dies geschah in 29 % bei einer Serie von 419 retrograden perkutanen Aortographien Diese Komplikation kam nur bei Fallen von Aortasklerose vor

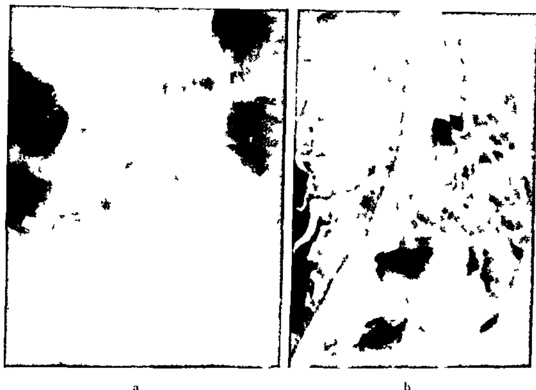


Fig. 2 a) Tubular deposition of contrast medium beneath the intima simulating total obstruction. Appearances unchanged in all the films of the series. No collaterals present. b) 2 days later, same technique. No occlusion of the aorta but thrombosis at the level of the origin of the left common iliac artery.

However, it is important to remember that all the complications in our series occurred in patients with preexisting clinical signs of arterial wall abnormalities. When calculated on the basis of this group of patients alone, the incidence is no less than 29 %. This supports our view regarding the pathogenesis of this injury, viz. that the catheter is caught by an arteriosclerotic plaque, passes beneath it, and then proceeds below the intima for a shorter or longer distance, the injury always occurs in the region of the tip of the catheter from which a major or minor intramural spread of contrast medium is evident. *This assumption receives further support from the fact that in 27* out of the 36 cases of damage, there had been difficulties in inserting the catheter (slight resistance to the insertion or inability to pass the catheter to the desired level). That the injection was nevertheless performed appears to have been due to the occurrence of a free reflux of blood from the catheter prior to the injection of the contrast medium and to the contralateral femoral artery not being accessible to puncture.

All the investigations were carried out by the same slightly modified Seldinger technique. The number of intimal injuries was evenly distributed among four *different* examiners.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF ERIK LINDGREN) SERAFIMER LASARETTET STOCKHOLM SWEDE

CONVERTIBLE CHAIR COUCH FOR ROENTGEN EXAMINATIONS

by

ERIK LINDGREN

The development of the Mimer recently described by FREDZELL & LINDGREN was prompted by the need for a unit which would offer more facilities in modern neuroradiologic work than the Lysholm skull table A need has also been felt for an improvement upon the patient table The one employed with the old unit has not been found satisfactory as in practice it permits an examination to be performed with ease only with the subject recumbent, and considerable inconvenience has been connected with its use when the patient had to be examined in the sitting position The correct procedure in encephalography demands that the patient be examined in the sitting position during the initial stages of the examination but it is also desirable that the change in position from the sitting to the horizontal can be easily performed as the examination proceeds It may still happen despite adequate premedication that a patient faints while sitting upright during an examination and for this reason it is also important to be able to lower the patient easily and carefully It would obviously be an advantage and also minimize the risk of fainting, if the first part of an encephalographic examination could be performed without having the patient sitting upright Attempts have been made, e g by LENZI, to dispense with the sitting position by placing the patient on a more or less

Submitted for publication 15 August 1960

RÉSUMÉ

Les auteurs signalent la frequence des lésions de l intima suivies de dépot de moyen de contraste dans la paroi vasculaire, dans 29 % des cas d une serie de 419 aortographies rétrogrades percutanees abdominales Cette complication ne s est produite que dans les cas d arteriosclérose mais pas dans les autres affections

REFERENCES

BOBLITT D E FIGLEY M M and WOLFMAN L I Roentgen signs of contrast material dissection of aortic wall in direct aortography Amer J Roentgenol 81 (1959) 826

GAYLIS H and LAWS J W Dissection of aorta as a complication of translumbar aortography Brit Med J 2 (1956) 1141

McAFEE JOHN G A survey of complications of abdominal aortography Radiology 68 (1957) 825

SELDINGER S I Catheter replacement of the needle in percutaneous arteriography A new technique Acta radiol 39 (1953) 368

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF ERIK LINDGREN), SERAFIMER LASARETTET STOCKHOLM SWEDEN

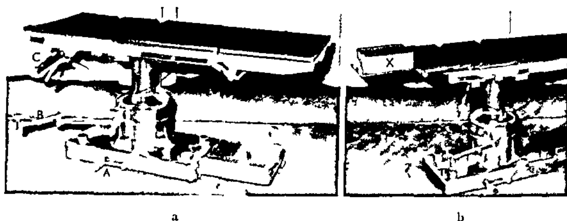
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a b

Fig 1 a) The chair couch adapted for the recumbent position A — Foot brake B — Foot operated control for raising or lowering the top C — Handle for the adjustment and locking of the top longitudinally and transversely D 1 1 G — The four sections of the top of the couch or the parts of the chair b) The head rest (X) attached

steeply inclined tilting table No methods of this type would appear, however, to permit the establishment of a satisfactory encephalography

Encephalography is probably carried out in most departments in the following manner The patient is first placed astride an ordinary chair with the arms across its back and the forehead against the skull table After the examination in the sitting position has been concluded the patient is transferred to the conventional table for the further stages of the examination There are many drawbacks attached to this procedure particularly if the patient is unconscious or under general anesthesia

An examination chair of the kind described by the present author in 1957 was used for some considerable time in the roentgen department of Serafimer lasarettet The patient was seated in this chair, with rubber padded supports pushed against the armpits and with further supports for the forearms The chair, the height of which was adjustable, was placed in front of a Lysholm skull table, fixed vertically, against which the forehead of the patient rested A strap could, if necessary, be stretched between the armpit supports to prevent the patient from falling backwards The patient s feet were placed on a foot rest The chair proved satisfactory in holding the patient firmly At the conclusion of the first stage of the examination, the chair, with the patient still in the sitting position, was wheeled over to the ordinary table and placed in such a way that the seat of the chair was at a slightly higher level than the table top, the patient could then be moved over and laid on the table by lowering one of the arm supports of the chair The seat could remain under the patient as it was readily detachable from the rest of the chair Although this chair possessed many good points it was not ideal It may, however, be regarded as a prototype which led to the design and construction of the present convertible chair couch Dietrich

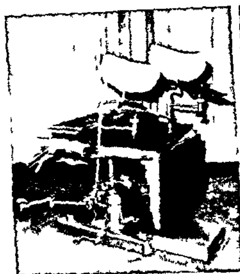


Fig 2 The convertible chair-couch with arm supports attached and adapted for the sitting position



Fig 3 *Operator and patient during lumbar puncture the patient's forehead rests against the vertically fixed object table of the Mimer*

in 1959 described a similarly combined unit the construction of which was based upon a gynaecologic table This permitted the patient to sit upright during the first part of the examination and to be lowered to the recumbent position by a few manual adjustments To judge from the description, however this unit seems to have many disadvantages

The general outline and construction of the new examination chair couch is shown in Fig 1 It is mounted on small wheels which lie protected below the base of the unit (and therefore not visible in the photograph) so that it is freely manoeuvrable the wheels can be locked by means of a foot-operated brake (Fig 1—A) The unit may also be raised or lowered by means of another foot pedal (Fig 1—B) When used as a couch the four sections are combined as one unit which can be moved 135 mm longitudinally and 90 mm transversely Small adjustments in the positioning of the patient in relation to the object table of the Mimer can therefore be effected without having to move the entire unit The adjustment and locking of the couch top are executed by means of a handle (Fig 1—C) A head rest may be attached to the head end of the couch if it is found necessary to move the patient while still on the couch, to another location

The section which represents the foot end of the couch top (see Fig 1) can be folded down or the section marked D may be turned up onto the top of section E or again these two sections may be pulled up together as a unit to form the back of a chair' while the patient remains seated on part F of the

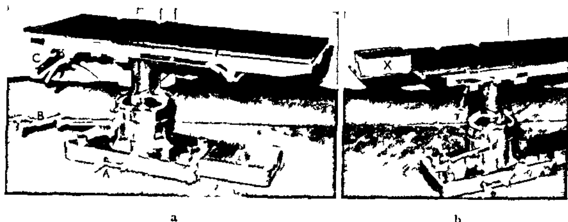


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The device for supporting the head of an unconscious patient (see Fig 5) is in principle the same as the one earlier described (LINDGREN 1957) This consists of a metal arm that can be mounted at the upper edge of the Mimer object table and upon which another T shaped adjustable arm is fixed Straps from the three free ends of the T arm are attached to a sling constructed like the so called Glisson sling This is applied around the neck and the chin of the patient and by varying the tension of the straps the head of the patient can be bent sideways or flexed to different degrees

Encephalography in the sitting position even in the case of a patient who is unconscious can thus be easily performed with the aid of the new examination unit and the necessary sling attachments An image intensifier may also be employed if it is considered desirable to study the passage of air It should be mentioned that the convertible chair couch may of course be used also with the Lysholm skull table

The convertible chair couch for roentgen examinations is now in production and is being manufactured by Elema Schonander Stockholm Sweden

SUMMARY

A convertible chair-couch which permits encephalography to be performed as easily with the patient sitting as in the recumbent position is described

ZUSAMMENFASSUNG

Ein Untersuchungsgerat convertible chair couch wird beschrieben Es ermoglicht die Encephalographie ebenso leicht mit sitzendem als mit liegendem Patienten durchzufuhren

RÉSUMÉ

Description d un fauteuil brancard transformable pour les examens radiologiques, permettant d exécuter une encephalographie aussi aisément que le malade soit en position assise ou couchée

REFERENCES

DECKER K Encephalographie am Bildwandler Fortschr Rontgenstr 87 (1957) 707

DIETRICH G Ein kombinierter Lagerungstisch fur sitzende und liegende Position am Lysholm Schadelgerat Rontgenblatter 12 (1959) 136

FREDZELL G and LINDGREN E Mimer Acta radiol 53 (1960), 209

LENZI M Eine neue Zisterno-encephalographische Technik Fortschr Rontgenstr 80 (1954) 479

— Zwei Jahre Erfahrungen unserer Cisterno-encephalographischen Technik Acta radiol. 46 (1956) 87

LINDGREN E Radiologic examination of the brain and spinal cord Acta radiol (1957) Suppl No 151



Fig 4 An unconscious patient in the chair



Fig 5 Details of the fixation attachments for the head

'chair' The unit, with arm supports attached and adapted as a 'chair', is shown in Fig 3, the resemblance to our earlier examination chair is apparent The supports provided for the armpits and forearms are similar to the previous constructions They are adjustable both in height and in distance from each other so as to accommodate a patient of any build the supports are moved in place on rails which are fixed along the edges of the convertible chair couch

It will be evident from what has been stated previously that when the unit is used as a chair during an encephalography, the head section is not folded down, as is, for instance, the case with the table described by DIETRICH The head section in such a position would most likely be in the way of the examiner and hinder his movements when a lumbar puncture has to be performed Nevertheless the section may still fulfill a purpose by forming a small platform that can be used as an arm rest by the operator making the injection, or for holding kidney bowls or other objects that he may require at hand The respective positions of the examiner and patient at the commencement of an encephalographic examination are shown in Fig 3 When that stage of the examination during which the patient has to be in the sitting position has been concluded, the foot section (see Fig 2—G) is lifted up, section 'D' is moved to the same level as section 'E', and the patient can be laid down

substitution of rubidium and cesium for potassium It appears from a series of experiments (RELMAN et coll 1956) that skeletal muscle of rats accumulates the three cations at equilibrium in definite order of preference — cesium > rubidium > potassium Were rubidium and cesium more abundant in the crust of the earth, there is according to RELMAN, every reason to believe that they rather than potassium would be the chief cations of muscle tissue The order of preference may be of significance for the estimation of the radiation hazard from cesium 137

Cesium 137 is often referred to in terms of its danger as an external gamma radiation source Because cesium 137 is also a beta emitter, it is however, dangerous as an internal source of radiation Since the energy which it releases to tissues from its beta radiation is much greater than that absorbed from the gamma radiation the latter may be neglected for dosage estimation Consequently the distribution of cesium 137 in the different tissues of the body is clearly a matter of great importance

The tissue distribution of radionuclides may be investigated either by measuring the radioactivity with a G M or scintillation counter in samples of different tissues or by autoradiography In practically all previous studies of the tissue distribution of radiocesium impulse counting has been applied Several investigators (HAMILTON 1947 HOOD & COMAR 1953, BALLOU & THOMPSON 1957 RICHMOND 1958) have studied the distribution of radiocesium in rats at different intervals after administration It was found that the distribution was similar after oral and intraperitoneal administration Muscle, skin, gastrointestinal tract and liver were the tissues with the largest cesium accumulation shortly after administration The concentration in the blood brain and bone was relatively low Muscle and brain were unique in that maximum concentrations were not reached on the first day After the first day the muscle skin heart lungs testes and brain contained relatively constant fractions of the total body burden, but the bone gastrointestinal tract spleen liver, kidney and plasma contained diminishing fractions of the body activity Erythrocytes contained more cesium than plasma for some time after the first day On the first day the liver activity represented one seventh of that in the muscles A relative decrease of liver activity to only about one thirtieth occurred after some days

The transfer of cesium from mother to foetus in rats (HOOD & COMAR 1953) was also studied The concentration of Cs^{137} in the foetus was nearly constant throughout gestation (0 058 % dose/g) and there was apparently no foetal tissue accumulation

HOOD and COMAR also investigated cesium distribution in cattle sheep and pigs Muscle showed the highest accumulation followed by the viscera, brain, eye and endocrine glands The lowest concentration was seen in the blood bone and teeth The concentrations in various tissues were similar for all species including rats

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DISTRIBUTION OF RADIOCESIUM IN MICE

An autoradiographic study

by

ARNE NELSON, SVEN ULLBERG, HARRY KRISTOFFERSSON and CURT RONNBACK

Only a few radionuclides, among the great number of fission products produced at nuclear explosions, are of special significance with regard to internal contamination. Cesium 137, apart from strontium 90, is of particular concern because of its long physical half life of 26.6 years and its high fission yield.

Cesium 137 disintegrates to Ba^{137} of 2.6 min half life with the emission of two beta particles (92 per cent 0.52 MeV and 8 per cent 1.17 MeV). The lower energy beta particle is followed by a gamma ray of 0.66 MeV. Apart from its physical properties the potential hazard of an internally deposited radionuclide depends upon the period of retention and the distribution in the body. These properties reflect the significance of the element in the metabolism and in turn upon its chemical properties.

Cesium is an alkaline metal belonging to the same group as potassium and rubidium. These three elements have very similar chemical and physical properties. A review of the physiology of rubidium and cesium by RELMAN (1956) cites some evidence for the close similarity of the biologic effects of these ions to those of potassium, significant quantitative differences have been noted, however, between the physiologic behavior of these ions. Cells can distinguish between them and higher organisms will not indefinitely tolerate

Submitted for publication 10 October 1960

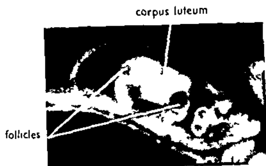


Fig 2 Detail from autoradiogram showing the ovary 15 min after intravenous injection of Cs in pregnant mouse Slight accumulation in corpus luteum

frozen animals were cut and dried in a freeze room at −10 C The autoradiographic exposure was made by apposition against Gevaert Dentus Rapid film The exposure time varied from 7 days for the shortest survival time to 84 days for the longest The autoradiographic method has been described in detail by ULLBERG (1954 1958)

Results

Because of the short biologic half life of radiocesium in mice the overall activity in the tissues decreases rapidly This has been compensated in our autoradiograms by a gradual increase in exposure time Satisfactory density was obtained in the autoradiograms from animals sacrificed up to 16 days after the administration of Cs^{137} while at 32 days the radiocesium content in most tissues gave a very low density

Shortly after injection the greatest activity is found in the cartilage, salivary glands kidneys and intestines Later the skeletal muscles and cartilage show the greatest activity

The distribution in different tissue groups at different intervals will be described below (see also Figs 1 to 7)

Blood The concentration of radiocesium in blood decreases very rapidly being lower than in the skeletal muscles by 5 min This decrease continues but more slowly and after 4 days there is scarcely any radioactivity observable in the blood

Bone muscle and skin The compact bone and the teeth show a low radio activity A somewhat higher uptake however, can be observed subperiosteally especially at the insertion of tendon A strong accumulation is at all times observed in cartilage and tendons especially in hyaline cartilage of the trachea and joints and also in the elastic cartilage of the epiglottis The fibrous cartilage of the vertebral discs however shows a low uptake

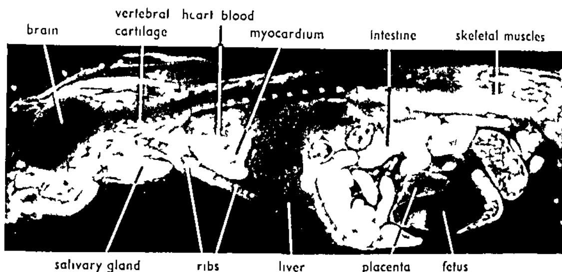


Fig 1 Autoradiograms showing the distribution of Cs^{137} in a pregnant mouse 5 min after intravenous injection White areas correspond to high radioactivity The Cs^{137} concentration is already higher in the myocardium than in the heart blood High uptake in cartilaginous parts of ribs and vertebrae and in salivary gland and intestine

Using a macroscopic autoradiographic method (NELSON 1957) the distribution of cesium 137 (NELSON & CARLQVIST 1958) was investigated at different intervals in rats from 5 min to 3 months after an intraperitoneal injection of 40 μC Cs^{137} A very high density was observed on the autoradiograms at 1 hour over the abdominal organs and heart No increased density could be seen in the skeleton or teeth The density on the first day was more even because of an increased density in the muscles By the third day the density of the muscle was still more prominent although the density of the thyroid and the tongue was about the same After one month the density, which had decreased considerably in intensity, was most evident in the skeletal muscles

The macroscopic autoradiographic method did not provide satisfactory information Hence in the present investigation a method has been used which gives a better resolution and makes it possible to scan the distribution of radiocesium in *practically all the tissues, organs and fluids of the body in* survey autoradiograms

Methods Sixteen mice of the CBA strain 8 adult males and 8 pregnant females, were injected in a tail vein with carrier free Cs^{137} chloride in physiologic saline solution to give an individual dose of about 0 2 μC/g bodyweight

One mouse of each sex was killed at 5 min, 15 min, 1 hour, 6 hours, 24 hours, 4 days, 16 days, and 36 days after injection by immersion in a mixture of solid carbon dioxide and acetone (— 78° C) The female mice were sacrificed 2 days before expected parturition Sagittal 20 μ sections through the whole



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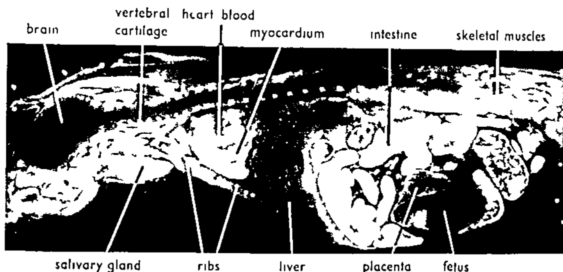


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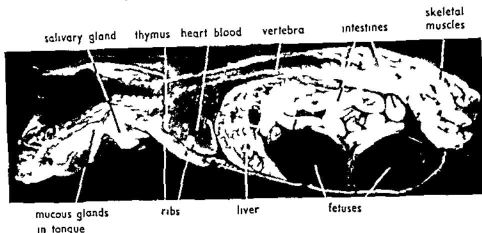


Fig 4 Autoradiogram showing distribution of Cs in a pregnant mouse 6 hours after intravenous injection Concentration in foetuses significantly lower than in the mother

Pancreas shows the same level of activity as the intestinal mucosa The islets of Langerhans appear to have a slightly lower activity than the acinar tissue

The liver has a consistently low and even concentration of radiocesium The activity in the biliary ducts at 15 min and 1 hour is slightly higher than in the liver but decreases later

Urogenital organs The kidneys show a high activity from 5 min to 6 hours after injection with a maximum at 15 min Subsequently the activity in the kidneys is only slightly higher than that of the liver

Initially during the excretory phase the activity is higher in the renal medulla than in the cortex The contents of the urinary bladder show a high activity during the first 24 hours

The testes and epididymis show an even and moderately high activity slightly higher than the liver but significantly lower than the skeletal muscles By 16 days the radioactivity in the testes is still relatively high (see Fig 7b) The ovaries of only two mice appeared in the autoradiograms In one animal killed after 15 min the ovary shows only a moderate activity with the highest uptake in the corpora lutea No activity however, is seen in the follicular fluid In the other mouse killed after 1 hour the concentration in the ovary is higher than in any other tissue except cartilage In this animal the activity is more evenly distributed in the ovary

Central nervous system With exception of the blood the brain and spinal cord show the lowest initial radioactivity in the body Subsequently, however the activity increases in relation to that in other tissues The distribution is rela

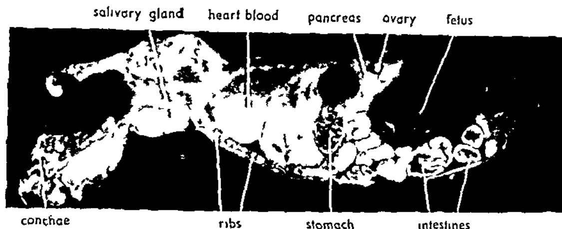


Fig 3 Autoradiogram showing distribution of Cs^{137} in a pregnant mouse 1 hour after intravenous injection High radioactivity in ovary

All skeletal muscles show a great uptake as early as 5 min after injection The density increases in relation to that in the other tissues, and from one day after injection and onwards the skeletal muscles and cartilage have the greatest cesium contents in the body There is an uneven distribution between different groups of muscles with the gluteal muscles showing the highest uptake

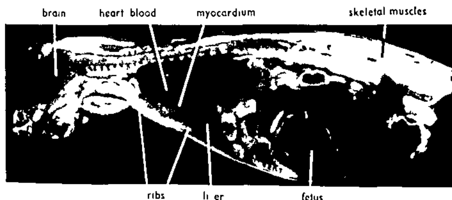
The myocardium initially shows a significantly higher activity than the skeletal muscles but by one hour this situation changes and subsequently the density in the myocardium is very low, only slightly higher than the blood level

The skin and the subcutaneous tissue show a moderately high uptake A high uptake is observed in the intrafollicular portion of the hair shafts

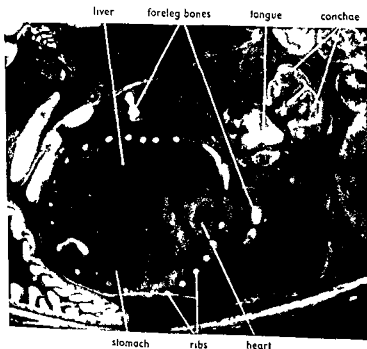
Respiratory organs The respiratory organs show a low activity with the exception of the cartilaginous structures

Digestive organs The only specific concentration in the oral activity is in the small mucous glands at the base of the tongue which have a high activity from one to 24 hours after injection The salivary glands together with cartilage and the kidneys initially show the highest activity in the body The accumulation in the salivary glands is very marked by as early as 5 min and remains so for 4 hours, but is significantly lower after 24 hours No activity can be observed after 4 days

The activity in the gastric mucosa and contents is low but in the intestinal mucosa and contents it is high from 15 min to 24 hours after injection By 5 min there is very high activity in the mucous glands of the colon From one to 24 hours there is a high activity in the contents of the large intestine followed by a gradual decrease



a



b

Fig. 6. a) Autoradiogram showing distribution of Cs in a pregnant mouse 4 days after intravenous injection. Radiocesium content is now much higher in skeletal muscles than in myocardium. Very low blood concentration. b) Detail from same animal as in (a) showing foetus. Specific uptake in foetal skeleton.

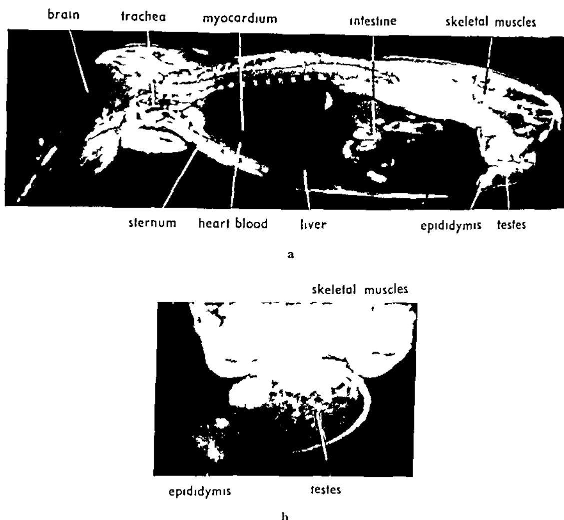


Fig 5 a) Autoradiogram showing distribution of Cs [?] in a male mouse 4 days after intravenous injection b) Detail from autoradiogram in (a)

tively even, the grey matter having a slightly higher activity than the white matter No accumulation is observed in the choroid plexuses

Eye A high uptake is seen in the sclera and the lens and a fairly high in the retina Unlike the salivary glands the lacrimal glands show no accumulation

Lymphatic tissues The activity in lymph nodes, spleen and thymus is slightly greater than in the liver and is evenly distributed The activity in the thymus of animals killed at 4 days and later appears relatively higher

Endocrine organs The activity in the pituitary is only slightly higher than in the brain The thyroid and the adrenals also show a low activity

Discussion

ım like potassium is taken up by the soft tissues against the concen gradient as already indicated by HOOD and COMAR (1953) and which rally explained as due to an intracellular accumulation

autoradiograms illustrate the rapidity of the disappearance of radio from the blood and the accumulation in the tissues By as early as after injection the blood level is lower than in most tissues

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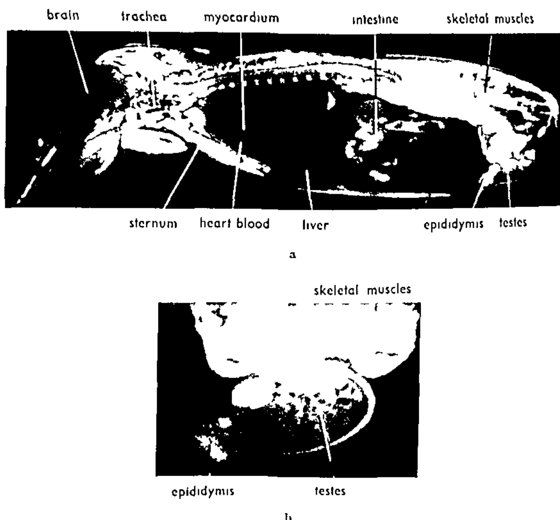


Fig 5 a) Autoradiogram showing distribution of Cs in a male mouse 4 days after intravenous injection b) Detail from autoradiogram in (a)

tively even, the grey matter having a slightly higher activity than the white matter No accumulation is observed in the choroid plexuses

Eye A high uptake is seen in the sclera and the lens and a fairly high in the retina Unlike the salivary glands the lacrimal glands show no accumulation

Lymphatic tissues The activity in lymph nodes spleen and thymus is slightly greater than in the liver and is evenly distributed The activity in the thymus of animals killed at 4 days and later appears relatively higher

Endocrine organs The activity in the pituitary is only slightly higher than in the brain The thyroid and the adrenals also show a low activity

Discussion

Cesium, like potassium is taken up by the soft tissues against the concentration gradient as already indicated by HOOD and COMAR (1953) and which is generally explained as due to an intracellular accumulation

The autoradiograms illustrate the rapidity of the disappearance of radiocesium from the blood and the accumulation in the tissues By as early as 5 min after injection the blood level is lower than in most tissues

The greatest radioactivity appeared in the cartilage, an observation which does not seem to have been made previously The uptake was very rapid which is astonishing with regard to the absence of blood vessels in this tissue The rapid uptake does not suggest accumulation due to incorporation of cesium into an organic compound An autoradiographic investigation of the distribution of Na^{22} has also shown a higher accumulation in cartilage than in other tissues (HUGGERT, ODEBLAD, SOREMARK & ULLBERG 1961) This may indicate that cartilage acts as a cation exchanger There is otherwise very little similarity in the distribution of Cs^{137} and Na^{22} The concentration of sodium remains high in the blood and unlike cesium, sodium accumulates in bone

With regard to the accumulation in muscles it is remarkable that the myocardium in spite of a high initial concentration does not show the property of the skeletal muscles of retaining cesium In addition to the tendency to penetrate into cells there must be some other explanation for the distribution in the muscular tissues

The fact that the foetus unlike the dam does not accumulate cesium in salivary glands kidneys or intestines may be explained by the low or absent excretory activity in the foetus The low radioactivity in the foetal muscles, in comparison to that in the maternal muscles is difficult to explain The fact that the concentration of cesium in the foetus is lower than that of the mother due to a partial placenta barrier is of importance when evaluating the radiation hazards This also applies to the fact that the concentration in the testes is not specially high but relatively consistent for a rather long period of time in comparison with other organs As regards the ovaries our material does not allow definite conclusions The high accumulation in the ovary in our animals may be explained by the fact that the animal was pregnant

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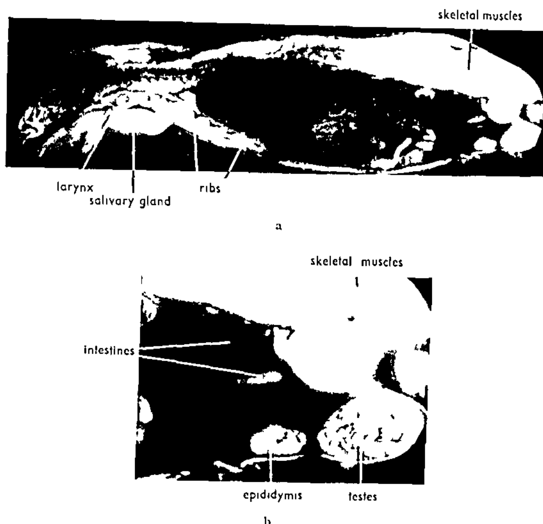


Fig 7 a) Autoradiogram showing distribution of Cs in a male mouse 16 days after intravenous injection Especially high retention in gluteal muscles and cartilage b) Detail from (a) showing male gonads Relatively high retention of Cs in testes

Foetus The activity in the foetuses at all intervals is considerably lower than that of the dam Some foetal uptake, however, can be noticed as early as 5 min after injection The distribution of the activity in the foetuses including the CNS is relatively even compared with the maternal distribution No specific accumulation is seen in the foetal skeletal muscles at 16 days Only the foetal skeleton, especially the tissues developing into definite cartilage, deviates by showing a higher uptake than the other foetal tissues

Placenta has an even concentration of radiocesium, greater than in the foetus and of about the same level as the liver of the dam Foetal membranes and fluids show a low activity

FROM THE INSTITUTE OF RADIOPHYSICS (DIRECTOR PROF R M SIEVERT), KAROLINSKA SJUKHUSET STOCKHOLM, SWEDEN

CESIUM 137 AND ITS GAMMA RADIATION IN TELERADIOTHERAPY

by

R THORAEUS

Up till now more than one thousand radioactive isotopes have been artificially produced and the properties of their radioactivities are fairly well known Among them however only a very few have attracted interest as regards radiotherapy application One of these few is Cs^{137}, and the reasons for it holding such a position are undoubtedly the monoenergetic gamma radiation emitted and its comparatively long half life (Cs^{137} has by far the longest useful life of any of the artificially produced gamma radiating isotopes available in large quantities) There are however certain disadvantages in its use

Cs^{137} was discovered during the late 1940 s by 1950 the characteristics of its radioactivity were fairly well known and the possibilities of separating sufficient amounts were under investigation It is well known that this isotope is produced by fission of U^{235} in the uranium fuel rods of atomic energy reactors The fission products are accumulated in the fuel rods and must be removed from the fuel periodically to maintain efficiency Cs^{137} is thus a true waste product The rapid development of nuclear reactors is now expected to make available large quantities of this material at a relatively low price in the near

The material contained in this paper was presented to the Meeting of the Nordic Society for Medical Radiology at Bergen Norway 10 to 11 June 1960
Submitted for publication 15 May 1960

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Les auteurs ont étudié la distribution du caesium 137 sur des coupes totales de souris males et de souris femelles gravides par autoradiographie à differents intervalles apres l injection

REFERENCES

Ballou J E and Thompson R C The long term retention of cesium in rat following a single intraperitoneal injection Hanford Works Report HW 46150 1957

Hamilton J G The metabolism of the fission products and the heaviest elements Radiology 49 (1947), 325

Hood S L and Comar C L Metabolism of cesium 137 in rats and farm animals Arch Biochem 45 (1953) 423

Huggert A Odeblad F Soremark R and Ullberg S Personal communication

Nelson A An improved method for macroscopical radioautography Acta radiol 47 (1957) 199

— and Carlqvist B Strålningsriskerna från cesium 137 (Swedish) Svenska Lak Tidn 55 (1958) 608

Relman A S The physiological behaviour of rubidium and cesium in relation to that of potassium Yale J Biol Med 9 (1956) 248

— Lambie A J Roy A M and Burrows B A The nature of the cation accumulation by muscle cells the displacement of potassium by rubidium and cesium Clin Res Proc 4 (1956) 150

Richmond C R Retention and excretion of radionucleides of the alkali metals by five mammalian species Los Alamos Scientific Laboratory Report LA 2207 1958

Ullberg S Studies on the distribution and fate of S^{35} labelled benzylpenicillin in the body Acta radiol (1954) Suppl No 118

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RELMAN, A S The physiological behaviour of rubidium and cesium in relation to that of potassium Yale J Biol Med 9 (1956) 248

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RICHMOND C R Retention and excretion of radionucleides of the alkali metals by five mammalian species Los Alamos Scientific Laboratory Report LA 2207 1958

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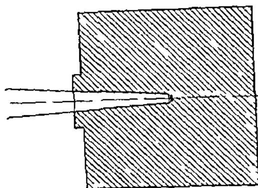


Fig 2 Schematic presentation of the cylindr c lead conta ner housing the cesium source

move when the source is subjected to vibration All sources must be rigorously tested to ensure freedom from leakage and from surface contamination

The radioactive decay is shown in Fig 1 Cs^{137} emits beta particles with energies of 1 2 and 0 51 MeV The latter beta emission results in an excited state of Ba^{137} which in turn decays to its stable state in emitting a monoenergetic gamma radiation of 0 662 MeV energy The beta emission occurs to 92 % via the excited state and 8 per cent directly to the stable state The decay from the excited state occurs to 89 % as gamma radiation, and the remainder as internal conversion electrons

The half life of Cs^{137} is stated to be 30 $\pm$ 3 years This means that the decay rate is approximately 1 5 % per year As far as radiotherapy is concerned, decay corrections of the dose rate may thus be spaced at at least one year periods

As already mentioned the specific activity of the salt is about 20 curies per gram Due to the production process of Cs^{137} the figures mentioned are considered as maximum values which cannot at present be increased Comparing some of the most important radioactivity characteristics of Cs^{137} and Co^{60} it is of particular interest to note that the gamma emission in rhm per curie of cobalt 60 is about 3 5 times as high as that of Cs^{137}, and further that a considerable increase in specific activity of the Canadian Co^{60} material from 35 curies per gram in 1956 to a maximum of about 150 at present, has occurred

Due to the relatively low specific activity it is not possible to produce kilocurie sources of Cs^{137} material with such small diameters as for example those of Co^{60} (1 5 to 2 cm) The dimensions of a Cs^{137} source for a given radiation output will thus be large compared with Co^{60} For example, a 1 000 curie Cs^{137} gamma source will be 2 5 to 3 0 cm in diameter and 3 to 4 cm in height

The long half life of Cs^{137} is a great advantage but it is usually accepted without regard to the Cs^{134} isotope which is produced by the same process and

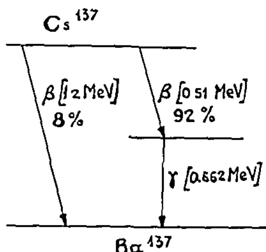


Fig 1 Radioactive decay of Cs^{137}

future BRUCER seems to have been the first to have discussed thoroughly the problems of radiotherapy by means of Cs^{137} gamma radiation from kilocurie sources (1, 2, 3, 4) He has characterized this isotope as 'a very important radiation source for future radiotherapy

Radioactivity characteristics of Cs^{137}

We shall briefly review the available information as concerns the most important characteristics of Cs^{137} radioactivity

Cesium is not chemically stable in its metallic form and must therefore be produced in the form of a chemical compound with the requisite stability from both the chemical and radiation aspects For example, the nitrate cannot be used because it decomposes under the influence of intense radiation At present Cs^{137} material is commercially available in two chemical forms, $CsCl_2$ and $CsSO_4$

In the USA, radioactive cesium is produced at Oak Ridge as dry cesium chloride powder This powder is then pressed to form compact pellets with a density of about 3 3 g/cm³, containing 22 curies of Cs^{137} per gram of solid The pellets are made in various diameters and doubly enclosed in welded stainless steel capsules

In the United Kingdom radioactive cesium is produced at Harwell and Amersham as cesium sulphate This also is pressed into pellets to provide gamma radiation sources The specific activity is in the region of 18 curies per gram of cesium sulphate and the density of the compressed salt is approximately 3 g/cm³ The pellets are doubly encapsulated, first in a 10 % iridium platinum liner which in turn is contained in a Monel metal source holder, both being sealed with a hard silver solder

The radioactive pellet must fit into the source holder closely enough not to

Table 1

HVL of Cs^{137} gamma radiation

Reference	mm Cu	mm Pb	cm water	cm Al
NBS Circular 583 (1957)				
calculated	10.8	5.8	8.1	3.4
experimental	10.9	5.6		
HAYBITTLE and DALLISON (1958)	10.6	5.4	8.0	—
Radiations from radioactive atoms (1959)	—	6.0	8.0	—
BURNS et coll (1959)	10.9	5.3	7.8	—
THORAEUS (1959 to 1960)	11.0	5.8	8.2	3.5

any initial contamination by Cs^{134} had been essentially eliminated by its own decay The gamma radiation used was thus substantially that emitted by Cs^{137} The source was about 2 mm in diameter and housed in a cylindric lead container as shown schematically in Fig 2 The lead thickness was at least 9 cm i e about 15 half value layers in all directions around the beam

The radiation measurements were made using our substandard the properties of which have been described elsewhere (11, 16) The energy dependence is small enough to permit of such radiation measurements as are required for the satisfactory determination of half value layers A half value layer determined in this way can then be used to interpolate the corresponding calibration factor by which the measurements can be given in terms of the roentgen

In the case of a low exposure dose rate it is of great value to be able to increase the sensitivity of the instrument This can be accomplished by removal of the additional capacitor thus reducing the electrostatic capacitance In this way the response of the substandard unit to radiation is increased nearly five times The calibration factors for this version of the substandard instrument show the same small percentage change with radiation quality as the complete instrument

Attenuation measurements of Cs^{137} gamma radiation under narrow beam conditions were made in lead copper water, and aluminium The attenuation data are plotted in the semilogarithmic diagram shown in Fig 3 It appears from the diagram that the measurement results fit closely to straight lines as might have been theoretically expected in the case of a monoenergetic radiation The half value layers interpolated from the experimental results are 11.0 mm of copper 5.8 mm of lead 8.2 cm of water, and 3.5 cm of aluminium These values are compared in Table 1 with some values collected from other recent papers It appears that the agreement between the author s results and those obtained from the NBS Circular 583 (9) is very good in most cases being almost within the measuring accuracy of the substandard

Measurements of Cs^{137} gamma radiation can accordingly be made with a

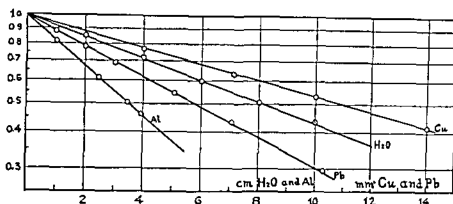


Fig 3 Attenuation measurements for HVL determinations

thus exists more or less as a component in the radioactive cesium material This component has a much higher gamma radiation emission per curie than Cs^{137}, but a correspondingly much shorter half life, about 2 3 years, and is therefore usually *considered as a contamination in the radioactive material*

Cs^{134} gamma radiation is not monoenergetic, but has a number of energies, some of which are not very far from that of Cs^{137} There is, however, also a small amount of gamma component the energy of which is practically the same *as that of cobalt 60 A contamination by* Cs^{134} *will thus hardly impair* the quality of the radiation from a therapeutic point of view But the important effects to be expected during the first years are a more rapid decrease of the exposure dose rate, and a temporarily somewhat higher rate of leakage radiation through the protection barriers, particularly that of the source head

It is said that the Cs^{134} contamination in new cesium sources may amount to as much as 15 %, but usually it is much lower, some 5 to 8 % or less In the case of considerable contamination the first half life of the material will never reach the 30 years value expected from Cs^{137}, but will occur far short of this value In fact, the first half life of such a cesium source may not be significantly greater than that of a cobalt 60 source

Radiation measurements

As the clinical use of Cs^{137} gamma radiation is expected to be introduced at *Radiumhemmet quite soon, and as the first and fundamentally most im*portant prerequisite for a proper clinical use of an ionizing radiation is its correct measurement, it was considered to be a matter of importance to study the properties of this radiation in advance A point of particular interest in this connection is the fact that the gamma radiation emitted is monoenergetic

The cesium *gamma radiation* used *in this investigation was obtained from* a source the age of which was about 8 years This means that the influence of

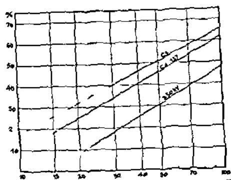


Fig 5 Comparison of percentage depth dose at 10 cm depth using three different radiations

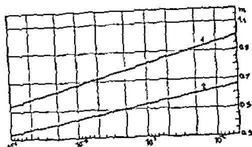


Fig 6 Attenuation factors for Cs gamma radiation in different thicknesses of ordinary concrete (1) and iron-ore concrete (2)

the references 10 and 11 have been plotted in the diagram shown in Fig 4 It appears that the depth of the build up region of Co^{60} is about three times greater than that of Cs^{137}

Considerations of the physical and radiation properties particularly the comparatively low specific activity seem at present to indicate certain limitations such that Cs^{137} radiation may be expected to be most suitable for those types of therapeutic application in which moderate focal distances of 20 to 35 cm are used A similar opinion has recently been stated by JOHNS (12) from his experience with a 1 300 curie source

However at such short focal distances as those below 35 cm the high penetration of the radiation cannot be appropriately utilized to produce its best possible percentage depth doses BRUCER (4) has studied the central axis percentage depth dose at 10 cm depth in water as a function of the source skin distance using three different radiations All the beams were defined by a fixed field size of 4 × 6 cm at a distance of 30 cm from the source The results are shown in Fig 5 and refer to the radiations Co^{60} gamma, Cs^{137} gamma, and 250 kV constant potential roentgen radiation

In the current literature there have as yet been very few observations published as regards the biologic reactions produced in the human skin and tissues by cesium 137 gamma radiation COMAS and BRUCER (6) however have recently reported their first impressions of therapy with this radiation using a kilocurie teletherapy machine at the Medical Division of the Oak Ridge Institute of Nuclear Studies This machine consists essentially of a shielded 1 500 curie cesium 137 source capable of movement in four directions tilt vertical horizontal and circular Very short collimator skin distances can be used in setting up stationary portals Most patients were treated at a distance of 29 cm between the collimator and the centre of rotation and a distance of 60 cm between the source and the centre of rotation The radiation output was 15 r/min at 60

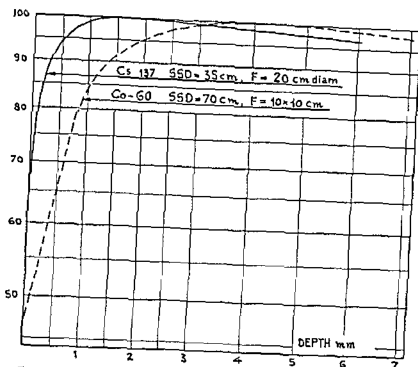


Fig 4 Comparison of build up regions for Cs^{137} and Co^{60} radiations

reliable ionization chamber unit, provided it has a small energy dependence over a wide range of half value layers, and is satisfactorily calibrated to such an extent that the factor for cesium radiation can be directly obtained, or safely interpolated in the calibration diagram

Clinically important properties

In studying the percentage penetration of Cs^{137} gamma radiation into the human body, the question of build up is of primary interest The existence of a build up region means a corresponding skin sparing effect which is of a great value in clinical work HAYBITTLE and DALLISON (10) have recently investigated this question by measurements at a source skin distance of 35 cm They found that (1) their beam was considerably contaminated with secondary electrons, (2) these electrons were effectively removed by a 0 5 mm thick filter of stainless steel, and that (3) maximum ionization with the filtered gamma radiation was attained at a depth of about 1 4 mm in tissue equivalent material

This result indicates that the build up effect of Cs^{137} gamma radiation is comparatively small The skin sparing effect obtained with this radiation is thus substantially less than that obtained with Co^{60} gamma radiation, in the case of the latter this effect is of paramount clinical importance To get a direct comparison, the build up regions of both Cs^{137} and Co^{60}, obtained from

present in the human body is only 30 % greater than for Co^{60}, the attenuation in substances of high atomic numbers used as protective material in the housing (source head) is 80 % greater than for Co^{60} Thus, although the penetration in the human body is not much reduced the problem of shielding the primary beam is notably reduced with Cs^{137} Due to this lead shielding and collimating is relatively more effective for gamma radiation from Cs^{137} than for that from Co^{60} In many cases where cesium sources are being considered lead lining can thus be used to advantage A cesium source can in fact, be housed in a shield the thickness of which is only two-thirds of that required for a cobalt source of the same radiation output

The equivalence between a monoenergetic radiation and a roentgen radiation consisting of a continuous range of radiation component energies a so-called bremsstrahlung, is sometimes considered this equivalence is then usually referred to the penetration It is evident, however that no real equivalence exists but a comparison may nevertheless be of interest and can be made without objection provided no particular conclusions are drawn from the results

Some results have been obtained using the half value layers given above Further results were given in a separate paper (17) in which the author has shown the special type of attenuation curves that are suitable for study of equivalence in penetration Using such curves it was possible to compare the attenuation in 3 8 iron-ore concrete of the monoenergetic gamma radiation from Cs^{137} with that of roentgen radiation of various peak energies The results have been collected in Table 2 and show that in this region of attenuation Cs^{137} gamma radiation has very nearly the same penetration as a roentgen radiation of 1 4 MV peak energy As far as penetration is concerned they may thus be considered equivalent in the region investigated It appears that the agreement is very good The region of attenuation factors 10^{-2} to 10^{-8} is of direct interest in radiation protection techniques

Conclusions

From the review now given and on the basis of the measurement results reported upon the following conclusions may be drawn

1 Due to the origin of Cs^{137} there are at present no practical means available to produce a material of very high specific activity, the maximum values seem to be about 20 curies per gram and a salt density of about 3 g/cm³ This means that sources of a suitable size for teletherapy can only be used at the comparatively short treatment distances of 15 to 35 cm At such distances however the penetrating power of the radiation cannot be fully utilized to produce its highest possible percentage depth doses There seem to be relatively few applications in which a short treatment distance would be desirable for its own sake

2 The general opinion appears to be that the clinical use of Cs^{137} is limited

Table 2

Comparison of penetration in various materials

Attenuation factor	Attenuator material	Thickness of attenuator	
		Cs^{137} gamma	1 4 MV roentgen
0 5 (first HVL)	Water	8 2 cm	8 3 cm
— —	Al	3 5 cm	3 6 cm
— —	Cu	11 0 mm	10 8 mm
10^{-3}	Iron ore concrete	35 cm	33 cm
10^{-4}	— —	43 cm	43 cm
10^{-5}	— —	53 cm	52 cm
10^{-6}	— —	63 cm	62 cm

cm, and the diameter of the source was 3 cm, giving an extensive penumbra that limited the concentrating effect of both the moving beam and multiple port techniques

The skin reactions observed were found to be similar to those occurring with cobalt 60 gamma radiation, except that in the case of cobalt the reactions usually occurred later The erythema produced by Cs^{137} gamma radiation was usually observed with a skin dose of approximately 2 000 r around the third or fourth week of treatment From the preliminary indications it would appear that a higher dose in comparison to cobalt 60 therapy can be given without the occurrence of excessive skin reactions, except around the mouth and pharynx where no difference was noted in the timing intensity, and the character of the reactions, as compared with those in 250 kV roentgen therapy or cobalt 60 therapy

Penetration and Protection

The most frequently used material for protection against high energy radiation is ordinary concrete Its density can be raised to about 2 4 by use of a mechanical treatment, called vibration The only disadvantage of this material is the comparatively great thicknesses required at radiations of high energy To reduce this disadvantage the use of iron ore concrete was introduced into the radiation protection technique by SILVERT (13) in 1933 In a later paper (17) the present author has described the modern production and properties of this high grade material from experience gained over the last few years Subjecting this material also to vibration, a density of 3 8 has been obtained A survey of the attenuation of Cs^{137} gamma radiation in different thicknesses of these two types of concrete is given in Fig 6 Curve 1 refers to ordinary 2 4 concrete and curve 2 to 3 8 iron ore concrete

As pointed out by BRUCER (4), an interesting advantage of Cs^{137} gamma radiation is that although the attenuation in substances of low atomic numbers

RÉSUMÉ

L auteur rappelle les caracteristiques de la radioactivité du cesium et en donne une comparaison partielle avec celle du cobalt. Il décrit la mesure de la radiation gamma du césium au moyen d un etalon secondaire dument étalonné et présente des résultats experimentaux en particulier les couches de demi absorption de certaines substances Il étudie certaines propriétés de cette radiation qui sont importantes pour la clinique la question de la radioprotection contre le cesium radioactif et le résultat de la détermination de l énergie de pointe de la radiation roentgen equivalente en pénétration a la radiation gamma du césium

REFERENCES

1 BRUCER, M New developments in teletherapy Nucleonics 10 (1952) 4 p 40
2 — Evaluation of teletherapy sources Nucleonics 10 (1952) 10 p 9
3 — Teletherapy design problems Radiology 62 (1954) 91
4 — An automatic controlled pattern cesium 137 teletherapy machine Amer J Roentgenol 75 (1956) 49
5 BURNS J E PERRY B J PIERCE N H et coll A kilocurie caesium 137 beam unit at Westminster hospital Physical aspects Brit J Radiol 32 (1959) 215
6 COMAS F and BRUCER M First impressions of therapy with cesium 137 Radiology 69 (1957) 231
7 FRANTZ F S and WYCKOFF H O Attenuation of scattered cesium 137 gamma rays Radiology 73 (1959) 263
8 GOODWIN P Calorimetric measurements on a cesium 137 teletherapy unit Radiat Res 10 (1959) 6
9 GRODSTEIN G W X ray attenuation coefficients from 10 keV to 100 MeV NBS Circular No 583 (1957)
10 HAYBITTLE J L and DALLISON J A cesium 137 gamma ray therapy unit Acta radiol *50 (1958) 321*
11 HULTBERG S DAHL, O THORAEUS R et coll Kilocurie cobalt 60 therapy at the Radiumhemmet Acta radiol (1959) Suppl No 179
12 JOHNS H E HUNT J W SKARSGARD L D et coll A caesium 137 teletherapy unit for use at a source to-skin distance of 35 cm Brit J Radiol 32 (1959) 224
13 SIEVERT R M On protection against radiation in teleradium treatment. Acta radiol 14 (1933) 597
14 SIMONS CH LAMPE I and LATOURETTE H B *The physical aspects of a cesium tele*therapy source Amer J Roentgenol 82 (1959) 587
15 SLACK L and WAY K Radiations from radioactive atoms in frequent use Nuclear Sci Abstr 13 (1959) 16 (No 14833)
16 *THORAEUS R* A substandard condenser dosemeter and its calibration against four national free air standard chambers Acta radiol 48 (1957) 473
17 — Iron-ore concrete in the radiation protection technique Acta radiol 54 (1960) 410

but that on the other hand its radiation may be well suited for head and neck applications particularly when the dimensions of the source head must be kept as small as possible. The use of tungsten heavy alloy (density about 18), or of uranium, may then be considered.

3. The build up effect of Cs^{137} gamma radiation is comparatively small, particularly when small source skin distances are used. The skin sparing effect of this radiation is, therefore, substantially less than that of Co^{60} gamma radiation, such an effect is in fact one of the big advantages of the latter.

4. The measurement of Cs^{137} gamma radiation can be done by means of a reliable ionization chamber unit with a small energy dependence over a wide range of half value layers, provided it has been subjected to a reliable calibration such that the factor for the cesium gamma radiation can be directly obtained, or safely interpolated in the calibration diagram.

5. One advantage of Cs^{137} gamma radiation is that less room protection is required than for a comparable Co^{60} unit. The primary beam requires only about two thirds the thickness of shielding of the cobalt 60 source. Furthermore, lead lining can be used to advantage since lead is relatively more effective for Cs^{137} radiation than for Co^{60} radiation.

6. The question of Cs^{134} contamination in the radioactive material of a cesium source is primarily of an economical nature and should thus be carefully considered. When a cesium source is to be ordered, it is recommended that a request be made for a guarantee of the percentage decay occurring in the first and second 5 year periods. This guarantee may then be compared to calculations based on a half life of 30 years. In case of considerable Cs^{134} contamination, a temporarily somewhat higher rate of leakage radiation through the protection barriers, particularly that of the source head, is also to be expected.

SUMMARY

A review of the characteristics of cesium radioactivity including partial comparison with that of cobalt is given. The measurement of cesium gamma radiation by means of an extensively calibrated substandard is described and the experimental results particularly the half value layers of some materials, are presented. Certain clinically important properties of the radiation, the radiation protection using radioactive cesium and the result of a determination of the peak energy of the roentgen radiation equivalent in penetration to the cesium gamma radiation are discussed.

ZUSAMMENFASSUNG

Es wird eine Übersicht über die charakteristischen Eigenschaften der Radioaktivität von Cesium gegeben und sie werden teilweise mit denen von Kobalt verglichen. Die Messung der Cesium Gamma Strahlung mittels eines umfassend geeichten Substandards wird beschrieben und experimentelle Ergebnisse besonders die Halbwertschichten von gewissen Materialen werden gezeigt. Gewisse klinisch wichtige Eigenschaften und der Strahlenschutz bei Verwendung von radioaktivem Cesium sowie das Ergebnis der Bestimmung des Scheitelwertes der Röntgenstrahlung die in Bezug auf Durchdringungsvermögen die Cesium Gamma Strahlung äquivalent ist werden diskutiert.

ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS. Volume VII Edited by C. A Tobias and J H Lawrence 562 pages 88 illustrations and 10 tables Academic Press New York 1960 Price $ 10

The present volume presents like the preceding ones, detailed reviews with extensive bibliographies of recent developments within selected sections of the vast domain of biophysics It also resembles the earlier volumes in that a large part of the space is dedicated to the uses of radiation and radioisotopes in research and to various radiation effects

The first paper by G S Stent and C R. Fuerst deals with the genetic and physiologic effects of radiophosphorus incorporated in viruses and bacteria It describes a number of beautiful experiments leading to the at first sight astonishing result that the effects considered are not primarily ordinary radiation effects of beta rays but effects caused by the disruption of DNA molecules when phosphorus atoms in the molecules are transformed into recoiling sulphur atoms

In the next paper by D Carlstrom apparatus and methods for roentgen-diffraction structure analysis on a microscale are described and examples of medical applications are given J H Taylor writes on autoradiography with tritium this contribution is noteworthy for the great resolution of the excellent films in which the activity in single chromosomes can be studied L E Lipetz reviews the electrical and chemical phenomena following optical or electrical stimulation of facet eyes of horseshoe crabs which for technical reasons are suitable for such studies The bearing of the results for an appreciation of corresponding processes in the eyes of higher animals and man is discussed

A paper by N N Livshits on the physiologic effects of radiation on the central nervous system is of particular interest. Mainly but by no means exclusively on the basis of Russian work various effects such as changes in conditioned and unconditioned reflexes EEG and the metabolism of different substances are reported in detail The central nervous system appears to be considerably more sensitive to radiation than was earlier assumed and in many cases unexpectedly low doses may produce significant effects.

D Gitlin and C H Janeway write on isotope studies of plasma proteins with emphasis on their own work with radio-iodine These experiments concern the diffusion of proteins between extra and intravascular spaces and their degradation under normal and pathologic conditions The last paper by L W Law deals with radiation carcinogenesis a subject of great topical interest due to the general concern over the possibly evil effects of radioactive fall-out and the medical use of roentgen radiation The author clearly shows the great difficulties in arriving at a well founded opinion in these matters and rightly criticizes the bold statements often scattered about.

While containing much more biology and medicine than physics the book should still prove most useful also to physicists interested in the subjects treated

Sten Benner

ERGEBNISSE DER WIRBELSÄULENFORSCHUNG Ausgegeben von H Junghanns. 140 Seiten 100 Abbildungen Hippokrates-Verlag Stuttgart 1960 Price DM 33

The book consists of papers of a congress and deals with the results of various investigations Biochemical and biophysical investigations of the intervertebral cartilages, the production of congenital deformities of vertebrae by experimental influences during foetal life (lack of oxygen roentgen irradiation) and movement studies of the cervical spine are among the subjects presented The results of advanced research are concerned more with the biology and pathology of the spine and not with clinical roentgen diagnostics

Folke Knutsson

BOOK REVIEWS

RISA ENCEPHALOGRAPHY AND CONVENTIONAL NEURORADIOLOGIC METHODS A COMPARATIVE STUDY By Giovanni Di Chiro 102 pages 38 illustrations 6 tables 60 sketches 3 diagrams Acta radiol (1961) Suppl No 201 Price Sw Kr 35 —

Conventional neuroradiologic methods (ordinary skull roentgenograms pneumography and angiography) are highly accurate for the detection and localization of intracranial lesions but not equally precise in determining the extent of the lesions Pneumography and cerebral angiography carry a low but definite incidence of morbidity and mortality and are a cause for discomfort to the patient It is therefore important to strive to find new diagnostic procedures

Collimated radioactive scintillation scanning of the head with RISA (radio iodinated serum albumin) has been used in more than 600 patients at the National Institute of Neuroradiological Diseases and Blindness (NINDB) to obtain information relative to the presence location and extension of cranial lesions To assess the reliability of this new method the results of examinations with RISA were compared with the results of conventional neuroradiologic studies in a series of verified cranial lesions

Tumoral lesions of the glioma group and in particular early and infiltrating gliomas missed by neuroradiology were detected with RISA Conversely some intracranial lesions detected by the conventional neuroradiologic methods were missed by RISA The latter was least helpful in cases of intra suprasellar and midline posterior fossa lesions Lesions situated laterally in the posterior fossa such as acoustic neuromas could on the other hand frequently be detected by RISA In determining the extent of some gliomas and occasionally also of other types of lesions RISA is sometimes more accurate than conventional neuroradiologic procedures The multiplicity of certain lesions (metastases meningiomas) which occasionally escapes the neuroradiologic methods is established with RISA At least at present however a certain degree of unpredictability is involved with the use of RISA since even large lesions may sometimes unexplainably be missed

Conventional neuroradiology remains unmatched for assessing the nature of the different lesions however

The procedure of RISA encephalography is harmless causes no discomfort to the patient and (after the initial expenditure) is not costly Because of the amount of information it offers RISA encephalography should not be regarded as a mere preliminary screening procedure It has the fullest qualifications for membership among the neuroradiologic methods and should be used as a complement to these

Autoreview

RADIATION BIOLOGY Proceedings of the Second Australasian Conference in Radiation Biology Melbourne 15—18 December 1958 Editor J H Martin 304 pages 86 illustrations and 50 tables Butterworths Scientific Publications London 1959 Price 69 Shillings

It has become almost a habit to print the proceedings of conferences in bookform Over saturation is imminent since scientific progress can hardly keep pace with the rate of publishing This statement should not restrain prospective purchasers of this book since it contains stimulating lectures and discussions on important problems of current research.

Although most branches of radiobiology and allied sciences were represented in the conference program two or three main themes predominated Two experienced radiobiologists were invited to give four lectures each this afforded the opportunity for a comprehensive treatment of their subjects to be made

L F Loutit from Harwell gave a well documented account of the radiation induction and treatment of leukaemia as well as the related fields of bone marrow transfer and its immunologic aspects This is a balanced and careful account of our knowledge which clearly sets out the many unsolved problems The present situation is that we cannot exclude the possibility that the experimental production of leukemia in animals is dose rate dependent and that high dose rates produce a higher yield of leukemia Mole as quoted by Loutit states there is no evidence to support the hypothesis that the chief determining factor in the incidence of radiation induced leukemia is dose and that there is some evidence from existing human data which denies the validity of extrapolation on the relation between dose and leukemia to situations where the dose intensity is very much less Two other lectures given by Loutit were devoted to the radioactive strontium problem and other radioactive isotopes in the food chain

What may be called basic radiobiology is another theme admirably treated by L H Gray Two of his lectures centred around the influence of oxygen on radiosensitivity and in the second he discussed future experimental possibilities which have been opened up by recent technical advance particularly the analyses of free organic radicals by electron spin resonance spectroscopy

The book consists of 29 lectures and discussions in all which also cover radiation chemistry, genetics and protection

A Forssberg

THE CELL NUCLEUS Proceedings of the 1959 Meeting at the University of Cambridge by the Faraday Society Editor J S Mitchell 269 pages, 115 illustrations and 38 tables Butterworths London 1960 Price 50 Shillings

The nucleus exerts a fundamental control of cellular function The mechanism by way of which this is maintained constitutes problems which need the joint cooperation of specialized workers in the fields of biophysics chemistry and the classical biologic sciences The present contributions to our understanding of this subject are the proceedings of an informal meeting at Cambridge The book is certainly one which requires a good deal of knowledge on the part of the reader the participants are leading workers in various relevant fields and the presentation of the material in short lectures and discussions is that of the specialist talking to fellow specialists in adjacent fields

In recent years great advances have been made towards a better understanding of the structure of chromosomes and the mechanism of the synthesis of the key substance deoxyribonucleic acid (DNA) The papers given at the conference centre round these and similar matters The reader obtains a fairly comprehensive view of the structure of the nucleolus and

RADIATION INJURY IN MAN ITS CHEMICAL AND BIOLOGICAL BASIS PATHOGENESIS AND THERAPY By E P Cronkite and V P Bond 200 pages and 18 illustrations Charles C Thomas, Springfield Ill 1960 Price $ 6 50

The aim of this book 'to fill a current need for a semi technical or non technical presentation of basic and practical material necessary for an understanding of the effects of ionizing radia tion in man is admirably fulfilled The design is the usual one basic physical and chemical information in introductory chapters followed by biologic and medical aspects The language is plain and descriptive mathematical formulas being avoided and technical terms explained in a glossary

The symptoms of irradiation injury are a function of the radiation dose, and any therapeutic measures are dependent on the dose received These facts are thoroughly discussed in chapters entitled The clinical picture of acute irradiation injury in man and Diagnosis and therapy of human radiation injury, practical considerations These are most useful by reason of the clinical approach which is not often found in current textbooks The authors discuss genetic and long term effects as well as the difficult question of the estimation of risks from fall out activity These are fields where the most divergent opinions have been expressed even by scientists Some of the difficulties arise because the statistical significance of biologic effects from low level radiation is in most cases low and the interpretation of the results is often open to question The authors wonder however and probably rightly whether disagreements may not also partly be occasioned by emotional, political and diplomatic considerations

A Forssberg

URETHROGRAPHIC STUDIES OF PROSTATIC TUBERCULOSIS By Niels Bentzen Thesis 114 pages and 45 illustrations Aarhuus Stiftsbogtrykkerie Copenhagen Denmark

The book is a thesis for a doctorate The title covers only about half the contents as detailed consideration is also given to relationship of renal tuberculosis to prostatic tuberculosis the role of the prostate in tuberculous bacilluria the treatment of prostatic tuberculosis and the pathogenesis of male genito urinary tuberculosis

The urethrographic studies comprise 155 cases of tuberculous bacilluria and a normal control series of 7 cases Exposures were made during and after injection and during mic turition

Abnormal filling of the prostate was found in 126 of the cases The cavities and possibly the ducts were filled in 99 cases while in the remaining 27 cases only the ducts were demonstra ted As the author emphasizes these findings do not necessarily indicate tuberculosis and the final interpretation must be based on the history and the clinical signs The follow up studies carried out during chemotherapy demonstrated a considerable improvement in the appearances although these never completely returned to the normal The illustrations adequately fulfill their purpose

The genetic radiation hazards involved in urethrography are considered These were found to be of only slight importance in the series under review as the majority of the patients were over 40 years of age and 38 per cent of them had a history of bilateral tuberculous epidi dymitis

In a general consideration of genito urinary tuberculosis the author expresses the opinion that prostatic, like renal involvement is a hematogenic phenomenon and of rather a different character from a direct spread to the ureter or bladder

Nils P G Edling

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its function in mitotic and metabolic activities Aspects of the synthesis of nucleic acids and the effects of irradiation on this process with particular reference to the autoradiographic technic as well as models of DNA structure as shown by various biophysical analyses are all discussed Occasionally the reader is faced with accounts of bold attempts to open quite new fields of research, as for example the cultivation of nuclei and chromosomes in vitro

In all the book offers stimulating reading about the basic aspects of life

A Forssberg

DIE ASBESTOSE DER LUNGEN Genese — Klinik — Rontgenologie Von H Bohlig G Jacob und H Muller 166 Seiten 97 Abbildungen Georg Thieme Stuttgart 1960 Price DM 66

This monograph is probably the most comprehensive and detailed analysis of asbestosis ever published and as indicated in the title deals with the genesis clinical aspects and roentgenology of the disease in addition to which the pathology and histology are described The chapter on the roentgenology of asbestosis forms the largest section of the book as might be expected The attempt to achieve a satisfactory division of the condition into stages is perhaps of greatest interest but it cannot be said that the authors have entirely succeeded Although they are in general agreement with Saupe s four stage division they state plainly that the first stage (0—I) is more or less impossible to diagnose and that the next stage (I) also causes great difficulties Stages II and III on the other hand may readily be determined from the roentgen findings with due consideration to the occupational history The division into stages is based wholly on the changes in the pulmonary parenchyma The pleural reaction is apparently considered by these authors to be one of the complications of the disease in spite of their observation that pleura thickening is observed post mortem in nearly all cases even in those with mild asbestosis (»Bei den Sektionsfällen wurden auch schon bei leichten Asbestosen fast ausnahmslos die Pleuraverschwartungen bestatigt«) It would appear to the reviewer that pleural reaction is a significant part of the clinical entity and produces disturbance of pulmonary function at an early stage the thickened pleura causes constrictio pulmonum with reduction of ventilation If this fact is not taken into consideration it is hardly possible to correlate the roentgenologic and clinical signs A division into stages on the principles followed by Saupe and the present authors is consequently of little practical value

The illustrations are of high quality but again the pleural changes are not sufficiently emphasized With the reservation mentioned which affects only a relatively small part of the contents the book is warmly recommended as a mine of information

Gunnar Jonsson

ACTA RADIOLOGICA

EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE FENNIAE NORVEGIAE ET SUECIAE

VOL. 55 JUNE 1961 FASC. 6

GROWTH AND DIFFERENTIATION OF THE POSTNATAL VERTEBRA

by

FOLKE KNUTSSON

The individual vertebra constitutes an element of the vertebral column a structure possessing static and dynamic functions It is the vertebral bodie built up into a pillar that bear the strain the function of the arches being limited to creating stability by restricting movement The development of the vertebra is consequently directed by biologic forces analogous to those determining the growth and conformation of the bones of the extremities The individual vertebra is also a unit in the structure of the spinal canal, which serves as a container for the spinal cord and its nerves and membranes It is therefore natural that the development of the vertebra is also influenced by the growth of the spinal cord

As our knowledge of the vertical and horizontal growth of the vertebral body is limited certain observations made by the author may prove of general interest

Vertical growth of the vertebral body

Exact figures concerning the growth of the long bones are available from previous investigations By measuring the distances between various points, marked on the growing bone with metal indicators it has been possible to

From the Roentgendiagnostic department (Director Prof Folke Knutsson) University Hospital Uppsala Sweden.

Submitted for publication 19 October 1960



Fig 1



Fig 2

Fig 1 *Horizontal venous groove (equator) at the middle of the surface of the vertebral body equidistant* from the superior and inferior surfaces of the vertebral body in a full grown individual

Fig 2 Second lumbar vertebra at 14 and 18 years of age intracancellous disk prolapse at anterior limbus edge persists as a hollow defect in the latest film The vertebral body has undergone general growth but the distance between the disk prolapse and posterior edge of the vertebral body remains unchanged The sagittal growth of the vertebral body has thus taken place only anteriorly

study the increment in length and arrive at the rate of growth Corresponding data on the increment in size of the vertebral body, however, do not appear to be available The embryonic development of this structure is well known but its subsequent growth during childhood and adolescence has never been mapped out in detail It is accepted that the increase in height takes place in the zone of ossification between the vertebral body and the cartilage plate, i e from two different directions, although it is uncertain whether or not the growth from the upper and lower surfaces is uniform

MOSER has reviewed the investigations that have been carried out in the past with the object of studying the increase in height The usual method has been to bring about a mechanical or radiation injury to a given area, and then to examine its effect upon growth The experiments were usually made in animals, and damage inflicted to both the intervertebral cartilage and the two adjacent vertebral body surfaces resulted in inhibition of growth In his own experiments in pigs, MOSER refined the technique by producing an injury affecting the upper surface of one vertebral body and the under surface of



Fig 3 The position of the dorsal layer of the cortex of the spinal canal is indicated by a metal thread which in the true lateral view is projected onto the middle of the inferior articular processes The sagittal diameter of the spinal canal is measured from the posterior surface of the vertebral body to the outline of this layer (Compare figs 5 and 6)



Fig 4 Vertebrae from a case of acromegaly Periosteal growth takes place chiefly anteriorly but not posteriorly (From ERDHEIM's work)

Fig 4

another This isolated investigation resulted in inhibition of growth of only that vertebral body of which the upper surface had been damaged MOSER concluded that the intensity of growth was therefore greater at the upper than the under surface of a vertebra The final result may hardly be regarded as reliable however because it cannot be established that the degree of trauma was equal at both sites MOSER also examined the thickness of the zones of ossification at the upper and under surfaces in postmortem specimens from children up to 10 years of age and found that the zones at the upper surfaces were always the thicker He concluded that this dissimilarity indicates that growth is livelier at the cranial than at the caudal surface

I would suggest that there is an indication that growth is equal at both upper and under surfaces of the vertebral body At birth the lateral roentgenogram reveals a translucent equator encircling the cylindric vertebral body and dividing it into an upper and lower half (Cf Fig 5a) The morphology of this equator has been investigated by HANSON who showed it to be a groove containing a venous sinus situated under the perichondrium which as development proceeds becomes less and less obvious and finally disappears altogether HANSON states that it may persist up to 14 years of age Vestiges of the groove may occasionally be seen in the adult and in such cases I have found it to lie equidistant from the upper and under surfaces of the vertebral body (Fig 1)

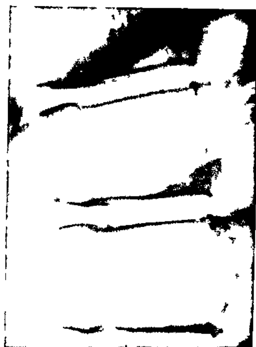


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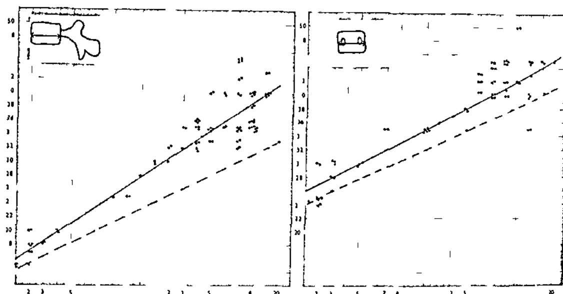
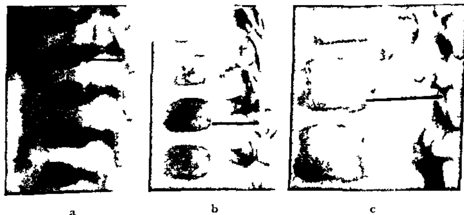


Diagram 1 Frontal and sagittal measurements of the vertebral body in 175 cases The age in years *is given on the abscissa and the size in mm on the ordinate The continuous lines represent the mean* of the values obtained the interrupted lines the true measurements after approximate correction for enlargement The vertebral body grows continuously throughout the entire growing period

the same appearance is apparent in HANSON s illustrations If growth had been more rapid at the upper surface, as MOSER claims, the groove in the adult ought reasonably to have become displaced towards the lower surface The matter would appear to require further investigation

Horizontal growth of the vertebral body

After the completion of endochondral ossification, growth of the vertebral body takes place by *means of periosteal apposition, with the interesting* feature that it is not equal all around the cylinder but takes place only at the front and



a b c

Fig 5 Spinal canal at different ages a) Neonate b) 3 months c) 2 years



Fig 6 Spinal canal at different ages a) 3 years b) 18 years

sides In a few cases I have been able to trace the development of a vertebral body by utilizing an unusually early intraspongious disk prolapse as the point of orientation It was observed that growth was taking place anteriorly but not posteriorly The case illustrated in Fig 2 is taken from a previous paper (KNUTSSON) The absence of growth posteriorly towards the spinal canal with consequent non encroachment upon its lumen during the course of growth of the vertebral body may be noted

In this connexion it is appropriate to consider the periosteal ossification that takes place in acromegaly ERDHEIM has demonstrated that this condition brings about a continuation of the normal growth process in the vertebral column the continued periosteal ossification resulting in apposition of new bone to the curved surface of the vertebral body this additional bone is thickest anteriorly is slightly thinner on the lateral surfaces and is absent on the posterior surface (See Fig 4)

The transverse and sagittal measurements of the body of the first lumbar vertebra were determined from roentgen films of 175 normal individuals aged between 1 and 20 years The findings are given in Diagram 1 The continuous line represents the mean of the values the interrupted line which represents the true measurements being obtained by making an approximate correction for the enlargement It will be clear from the diagram that growth takes place continuously throughout childhood and adolescence as long as the individual is still growing The vertebral body thus grows in the same manner as the extremities

Development of the spinal canal

The first lumbar vertebra was again selected for the study of the development of the dimensions of the spinal canal during the growing period, the trans

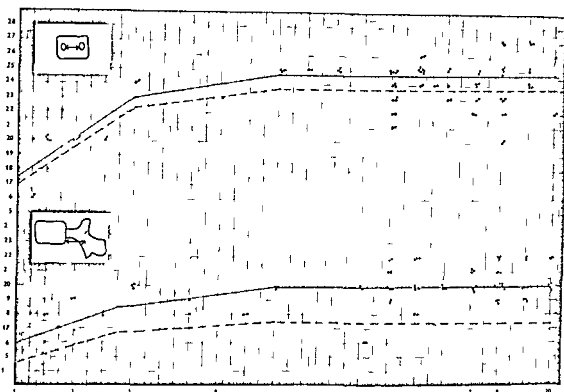


Diagram 2 Dimensions of the transverse (upper curve) and sagittal (lower curve) diameters of the spinal canal at varying ages (175 individuals) The age is plotted along the abscissa and the distance in mm along the ordinate The continuous lines represent the mean of the distances as measured in the roentgen films the interrupted lines the same values after approximate correction for enlargement viz the true dimensions The lumen of the spinal canal is already considerable at birth It increases rapidly in size up to the age of about 5 years and continues to enlarge slowly up to the age of about 10 years after when no further increase takes place

verse and sagittal diameters of the spinal canal being determined from roentgen films of 175 normal individuals of various ages

The *transverse diameter* of the spinal canal was obtained by measuring the interpedicular space Similar measurements have been published by FRENCH & PEYTON, SIMRIL & THURSTON, and SCHWARZ These writers reported the maximum dimensions in a series of normal growing individuals, figures which are required in order to establish the presence of pathologic measurements in the diagnosis of an intraspinal tumour

The *sagittal diameter* of the spinal canal was determined by measuring the distance between the posterior surface of the vertebral body and the inner cortical layer at the most dorsal part of the arch This limit is often clearly seen as an arcuate outline in the middle of the superimposed images of the inferior articular processes (Figs 3, 5 and 6)

The measurements obtained of the transverse and sagittal diameters of the

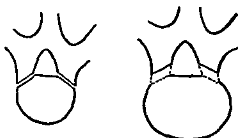


Fig 7 The growth of the vertebral arch springs from the cartilaginous bridge between it and the vertebral body the two halves of the arch fusing at the age of 1 to 2 years. Subsequent growth at the cartilaginous joint may result in enlargement of the transverse and sagittal diameters of the spinal canal

spinal canal are reproduced in Diagram 2 The continuous line is the mean of the individual figures the interrupted line being the mean of the figures after approximate correction for enlargement This latter line therefore represents the true measurements and its course will be an expression of the course of the development of the canal

The spinal canal is limited by the vertebral body as explained the vertebral body like the extremities, develops continuously throughout the growing period and as horizontal growth takes place only anteriorly and laterally the position of the posterior surface is established at birth It is therefore the growth of the vertebral arch that determines the development of the spinal canal The growth of the arch springs from the cartilaginous connexion with the vertebral body The two halves of the arch join by osseous fusion by the first or second year of life when the angle between them is established The arch may however be displaced backwards as a result of further growth at the cartilaginous junction subsequent extension of the peduncle continuing in the direction of the arch, in this manner the distance between the peduncles and the sagittal diameter of the spinal canal are increased (Fig 7)

The curves in Diagram 2 show that the dimensions of the spinal canal increase fairly rapidly from birth up to the age of 5 years and considerably more slowly between 5 and 10 years The canal is then fully developed and its lumen has reached its adult form The spinal canal has thus already achieved considerable dimensions at birth and little further increase takes place subsequently This rate of growth tallies fairly well with the information to be found in the literature, that is that the growth zone between the vertebral body and the arch gradually fuses during the 3rd to 6th years of life

It is of interest to compare the growth of the spinal canal with that of the cranial cavity The rate and pattern of growth of the cranium are determined by the development of the brain This latter is rapid in the fetus, and during the first 18 months of life, and a correspondingly rapid development of the cranium therefore takes place during this period After 18 months and up to 14 to 15 years the rate of growth is less (MacRae) The development of the spinal canal is evidently similar to that of the spinal cord This has already reached a

considerable stage of development at birth, and the lumen of the spinal canal has therefore achieved corresponding dimensions It continues slowly to widen during the first 5 years of life, and further, very slow, development takes place up to the age of 10 years, when growth is complete

SUMMARY

The vertical and horizontal growth of the vertebral body is described It is shown that the development of the spinal canal is determined by the growth of the vertebral arch It has already reached considerable dimensions at birth, in accord with the early development of the spinal cord

ZUSAMMENFASSUNG

Das vertikale und horizontale Wachstum des Wirbelkorpers wird beschrieben Es wird gezeigt dass die Entwicklung des Ruckenmarkskanales durch das Wachstum der Wirbelbogen bestimmt ist und schon bei Geburt ein betrachtliches Ausmass hat Dieser Umstand stimmt mit der fruhen Entwicklung des Ruckenmarks uberein

RÉSUMÉ

L auteur décrit la croissance du corps vertébral dans le sens vertical et dans le sens horizontal Il montre que le développement du canal rachidien est déterminé par la croissance de l arc vertébral et qu il a déjà atteint des dimensions considérables à la naissance, correspondant au développement précoce de la moelle épinière

REFERENCES

ERDHEIM J Über Wirbelsaulenveranderungen bei Akromegalie Virchows Arch path Anat 281 (1931) 197

FRENCH L A and PEYTON W T Mixed tumors of spinal canal Arch Neurol Psychiat 47 (1942) 737

HANSON R On the development of spinal vertebrae as seen on skiagrams from late foetal life to the age of fourteen Acta radiol 5 (1926) 112

KNUTSSON F Observations on the growth of the vertebral body in Scheuermann s disease Acta radiol 30 (1948) 97

MACRAE D L Die Krampferkrankungen *In* Klinische Neuroradiologie p 181 Her ausgeg von K DECKER Georg Thieme Stuttgart 1960

MOSER H Experimentelle Untersuchungen an den Wachstumselementen der Wirbelsaule *In* Die Wirbelsaule in Forschung und Praxis B 15 Hippokrates Verlag Stuttgart 1960

SCHWARZ, G S The width of the spinal canal in the growing vertebra with special reference to the sacrum Maximum interpediculate distances in adults and children Amer J Roentgenol 76 (1956) 476

SIMRIL W A and THURSTON D The normal interpediculate space in the spines of infants and children Radiology 64 (1955) 340

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (DIRECTOR PROF SOLVE WELIN), MALMÖ ALLMÄNNA SJUKHUS MALMÖ, SWEDEN

RELATIONSHIP BETWEEN 'ECCENTRIC CONTRACTIONS' OF THE GALLBLADDER AND THE POST-CHOLECYSTECTOMY SYNDROME

by

LARS ANDRÉN and GEORG THEANDER

ANDRÉN & THEANDER (1958) in a preliminary study of a characteristic type of dynamic deformation of the gallbladder or eccentric contractions during cholecystography with iopanoic acid (Telepaque) and its sodium salt (Bili jodon Natrium or Bi Na) found the sex and age distribution to resemble that of biliary disease The deformation occurred in 2 % (12 out of 536 cases) of males and 11 % (90 out of 815 cases) of females examined with Bi Na and in the latter most frequently in ages between 30 and 50 The figures were however based on observations made exclusively on satisfactorily demonstrated gallbladders containing no stones this qualification was made to attain a high degree of accuracy as large or numerous gallbladder stones may obscure the deformation

The roentgenographic appearances of eccentric gallbladder contractions will not be considered in this communication but an illustrative example is given on next page The phenomenon has been observed most frequently at examinations with the contrast media mentioned as well as with Orabilix, but only exceptionally with iodoalphionic acid Biligrafin and Biligrafin forte The present study was prompted by the similarity in sex and age distribution of biliary disease and eccentric contractions in examinations with Bi Na

It is well known that the abdominal discomfort and pain often experienced by patients with gallstones and attributed to the biliary system sometimes

Submitted for publication 23 January 1961

considerable stage of development at birth, and the lumen of the spinal canal has therefore achieved corresponding dimensions It continues slowly to widen during the first 5 years of life, and further, very slow, development takes place up to the age of 10 years, when growth is complete

SUMMARY

The vertical and horizontal growth of the vertebral body is described It is shown that the development of the spinal canal is determined by the growth of the vertebral arch It has already reached considerable dimensions at birth, in accord with the early development of the spinal cord

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Das vertikale und horizontale Wachstum des Wirbelkorpers wird beschrieben Es wird gezeigt dass die Entwicklung des Ruckenmarkskanales durch das Wachstum der Wirbelbogen bestimmt ist und schon bei Geburt ein betrachtliches Ausmass hat Dieser Umstand stimmt mit der fruhen Entwicklung des Ruckenmarks uberein

RÉSUMÉ

L auteur décrit la croissance du corps vertébral dans le sens vertical et dans le sens horizontal Il montre que le développement du canal rachidien est déterminé par la croissance de l arc vertébral et qu il a déja atteint des dimensions considérables a la naissance, correspondant au développement précoce de la moelle épinière

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ERDHEIM J Über Wirbelsaulenveranderungen bei Akromegalie Virchows Arch path Anat 281 (1931) 197

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HANSON R On the development of spinal vertebrae as seen on skiagrams from late foetal life to the age of fourteen Acta radiol 5 (1926) 112

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		Eccentric contractions Marked	Slight	Absent	Total
Postoperative course	Post-cholecystectomy syndrome	12	6	19	37
	Probably no symptoms	3	3	48	54
	No symptoms	0	2	17	19
	Total	15	11	84	110

It appears that the phenomenon occurred about four times more frequently *in the cases with postoperative symptoms than in those known to have become* symptom free The incidence observed in the former group though possibly reduced by the presence of gallbladder stones far exceeds the highest figure obtained in any series of examinations hitherto on record This observation is strengthened by the fact that 5 of the 12 cholecystographic examinations revealing marked eccentric contractions in this group were performed with iodoalphionic acid i e one of the contrast media least suitable for demonstrating the phenomenon

In those cases in which the postoperative course was not known with certainty the observed incidence of eccentric contractions was about the same as in those which had become symptom free

The findings suggest a close connection between the post cholecystectomy syndrome and so called eccentric contractions of the gallbladder They thus support the assumption which is not universally accepted, that biliary disease is responsible for the syndrome and indicate that cases of eccentric contractions of the gallbladder will probably not be relieved by cholecystectomy with removal of all stones

The physiologic and pathologic mechanisms underlying eccentric contractions of the gallbladder are still obscure The observations reported strongly suggest that some biliary dyskinesia is reflected by the phenomenon, and further work appears to indicate that the contractions observed are of a passive nature and due to a *maladjustment between the size of the gallbladder and the volume* of its contents This point is receiving attention and will be the subject of a future paper

SUMMARY

A study of preoperative cholecystograms of 110 cases which had been subjected to cholecystectomy and in which all obvious stones had been removed revealed that eccentric contractions of the gallbladder were far more common in cases with a post cholecystectomy syndrome

ZUSAMMENFASSUNG

Ein Studium praeoperativer Cholezystogramme von 110 cholezystektomierten Fallen bei denen alle feststellbaren Steine entfernt worden waren zeigte dass exzentrische Kontraktionen" der Gallenblase in Fallen mit einem Post Cholezystektomie Syndrom weit haufiger waren



Ro ntgenograms illustrating eccentric contractions in a gallbladder with stones.

persist after cholecystectomy and removal of any obvious stones from the bile ducts The condition, generally referred to as the 'post cholecystectomy syn drome, is widely considered to be due to some dyskinesia of the biliary system The possible connexion between this syndrome and the occurrence of eccentric gallbladder contractions on preoperative cholecystography was the subject of the present investigation

Material The preoperative cholecystograms of 110 cases, in which subsequent cholecystectomy with removal of any obvious stones was performed, were re viewed with special reference to eccentric contractions of the gallbladder In at least 19 cases, surgery had been followed by complete recovery but, in at least 37 cases, attacks of abdominal pain, probably biliary in origin, had recurred after operation The postoperative course in these 56 cases had been followed for from one to five years The course was probably favourable in most of the remaining 54 cases

Preoperative cholecystography had demonstrated the gallbladder satisfac torily and revealed the presence of gallbladder stones in every case With few exceptions the examinations had been performed with Bi Na Operative and postoperative cholangiography had demonstrated no residual stones Chole graphy with Biligrafin forte in cases with recurrence of symptoms had shown no signs of any pathologic condition

Results and Discussion

The incidence of various degrees of eccentric contractions observed in the preoperative cholecystograms as related to the postoperative course is shown below

FROM DEPARTMENT OF SURGERY I (DIRECTOR PROF E LJUNGGREN) AND DEPARTMENT OF PATHOLOGY II (DIRECTOR PROF S RANSTROM) UNIVERSITY OF GOTHENBURG SWEDEN

TOXICITY OF THE METHYLGLUCAMINE SALT OF TETRA IODOPHTHALIC ACID MORPHOLIDE

An experimental study in rats

by

Y EDLUND and L ZETTERGREN

The evolution of agents for the selective examination of the gallbladder has during recent decades passed from compounds containing one iodine atom bound to an aromatic nucleus to compounds containing three iodine atoms with the same nucleus This has resulted in the availability of a series of valuable diagnostic contrast media Compounds containing four iodine atoms in an aromatic ring constitute the next step a number of these are described in the literature although little is known about their toxic properties

Investigating the reaction between tetra iodophthalic acid anhydride and secondary amines SKAGIUS & EKEMARK prepared the methylglucamine salt of tetra iodophthalic acid morpholide (Ph 761/3 Pharmacia Uppsala, Sweden) In rabbits Ph 761/3 has shown promising properties as a roentgen diagnostic agent for intravenous cholegraphy (NOVEK) it produced a high content of iodine in the biliary flow although most of it was excreted via the kidneys It was deemed interesting in the light of these results, to study the action of Ph 761/3 on hepatic and renal tissues

Submitted for publication 14 October 1960

RÉSUMÉ

L étude des cholécystographies pré opératoires de 110 cas qui ont subi une cholécystec tomie et chez lesquels tous les calculs visibles ont été enlevés a montré que les contractions excentriques de la vésicule biliaire étaient beaucoup plus fréquentes dans les cas qui ont présenté un syndrome post cholécystectomie

REFERENCE

ANDREN, L and THEANDER G Eccentric contractions of the gallblader in cholecystography Acta radiol 49 (1958) 464

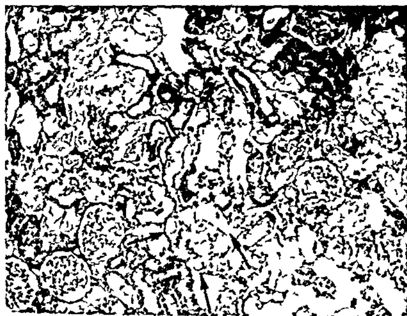


Fig 2 Kidney with granular and hyaline casts Haematoxylin — van Gieson

Results

Only one of the rats receiving 150 mg Ph 761/3 per 100 g bodyweight was examined post mortem In this animal as well as in the five given 75 mg per 100 g bodyweight the kidneys were pale yellow and flaccid In the group given 37 5 mg per 100 g bodyweight the kidneys were merely a little paler than normal In the two remaining test groups as well as in the control group the kidneys were macroscopically unchanged The liver was of normal appearance in all the groups

Microscopically the kidneys of rats given doses of Ph 761/3 exceeding 15 mg per 100 g bodyweight exhibited tubular degeneration (*nephrosis*) the degree of which varied roughly proportionally to the dose of the injected compound The convoluted tubules were mainly involved and, in severe cases were completely necrotic (Fig 1) Granular or hyaline casts were encountered in many of the convoluted tubules (Fig 2) both in those with destroyed and intact epithelium Moreover numerous casts were observed in the medullary collecting tubules in the advanced cases (Fig 3) No inflammatory changes were evident In no case were any changes found in the liver



Fig 1 Kidney with necrotic tubular epithelium Haematoxylin — van Gieson

Materials and Methods The investigation was performed in 29 albino rats belonging to the Sprague Dawley strain with an average bodyweight of approximately 200 g Ph 761/3 was administered by the intraperitoneal route in three consecutive daily doses, according to the following schedule

Dose per 100 g bodyweight	Number of rats
150 mg	5
75 mg	5
37 5 mg	5
30 mg	4
15 mg	5

Three of the rats that were given 150 mg per 100 g bodyweight died the day after the first injection, one on the day following the second injection, a fifth rat was killed two hours after the third injection All the other rats were decapitated on the fourth day i e the day after the third injection Five similar rats were used as controls They received three consecutive daily injections of 0 3 ml physiologic saline per 100 g bodyweight and were decapitated on the fourth day

The liver and kidneys were excised at necropsy, fixed in formalin 10 %, embedded in paraffin, sectioned, and stained with either haematoxylin — van Gieson or haematoxylin — eosine A few frozen sections were also prepared and stained with Sudan III

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BRANCHIAL ARTERITIS IN THE AORTIC ARCH SYNDROME

A roentgen and differential diagnostic study

by

N P G EDLING B NYSTROM and S I SELDINGER

SAVORY in 1856 published a paper dealing with a young woman in whom the main arteries of both upper extremities and of the left side of the neck were throughout completely obliterated This was apparently the first report of a disease which later by TAKAYASHU (1908) was suggested as being a pathologic and clinical entity Comprehensive studies on the subject including reviews of the literature have been published among others by ASK UPMARK (1954), ASK-UPMARK & FAJERS (1956) and KOSZEWSKI (1958) The number of cases which, rightly or wrongly are reported as examples of the disorder is about 150, about ten of them were confirmed by postmortem examination

The disease is characterized by a chronic progressive inflammatory process in the aortic arch as well as in the carotid subclavian and axillary arteries The etiology of the disease is unknown There is panarteritis with round cell infiltration in the periarterial tissues and all layers of the vessel wall Subsequent thrombosis frequently develops With few exceptions the condition is reported in young or middle aged females The symptoms and signs are both general and local the former including a high erythrocyte sedimentation rate (ESR)

Submitted for publication 19 December 1960

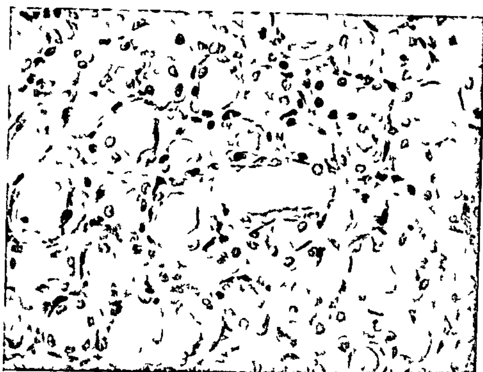


Fig. 3. Kidney with numerous hyaline casts in the collecting tubules. Haematoxylin — van Gieson.

SUMMARY

The toxic properties of a compound, the glucamine salt of tetra iodophthalic acid morpholide (Ph 761/3), that has shown promising properties as a roentgen diagnostic agent for intravenous cholegraphy in experimental animals, have been tested in 29 albino rats. The effects on the renal and hepatic tissues are described.

ZUSAMMENFASSUNG

Es wurde die Toxicitat des Glucaminsalzes von Tetrajodophtalsauremorpholid (Ph 761/3) die als Diagnostikum fur i. v. Cholegraphie im Tierexperiment vielversprechende Eigenschaften zeigte, an 29 Albinoratten getestet. Die Wirkungen auf die Gewebe der Nieren und Leber werden beschrieben.

RÉSUMÉ

Les auteurs ont étudié sur 29 rats albinos la toxicité tétra iodophthalique morpholide (PH 761/3) qui présente d'apres l'expérimentation animale des propriétés intéressantes comme moyen de contraste pour la cholégraphie intraveineuse. Ils décrivent les effets sur les tissus hépatique et rénal.

REFERENCES

NOVEK, JAAN: Excretion in the bile and urine of a biliary tract contrast medium. An experimental study in the rabbit. Acta radiol. 55 (1961), 359.

SKAGIUS, K. and EKEMARK, A.: Personal communication (1960).



Fig. 1. Case 1. Branchial arteritis. Heart and thoracic aorta. a) 20 years normal findings. b) 23 years. c) 27 years. Progressive dilatation of the aorta particularly of the ascending and arch portions. d) 23 years. Thoracic aortography. Thickening of wall of distal part of aortic arch (arrows) and irregular narrowing of uppermost part of descending aorta. The summits of the subclavian arteries and after a short course the right common carotid artery are occluded. Abnormal origin of markedly narrowed left common carotid artery from innominate artery near the aorta. Vertebral arteries probably normal. Collaterals present. Smooth contours.

in 8 of the cases, in addition in three of these cases a selective contrast injection into the left subclavian artery was made at the same sitting. Two bilateral and 4 unilateral arteriographies of the arms as well as one arteriography of the right innominate artery were performed. The femoral artery was examined by one bilateral and two unilateral arteriographies; in one of these the lower part of the abdominal aorta and the iliac arteries were also demonstrated. Thus in some of the patients, both aortography and peripheral arteriography were performed. The catheterizations were performed by the SELDINGER (1953) and ÖDMAN (1956) methods.

and the electrophoretic pattern of the serum proteins showing a slight or moderate increase of gamma globulins and hypoalbuminemia There is ischaemia in the region where the vascular supply is disturbed Headache, dizziness, fainting attacks, hemiplegia or aphasia, ocular disturbances, tiredness, and weakness in the arms with pain after exercise, may all occur Trophic changes in the carotid area with ulcers in the cutaneous tissues and nasal septum may also be seen The pulsations of the arteries distal to the affected portion are weak or absent A systolic murmur may be heard in the area of the stenosed arteries

Many names, such as Takayashu's disease, brachiocephalic arteritis, and pulseless disease have been given to the condition We shall use none of these for we prefer to term the condition branchial arteritis as suggested by KOSZEWSKI, this refers to both the *inflammatory character of the disease* and the peculiar localization in those arteries, including the aortic arch, which are derived from the embryologic branchial arteries Only very few exceptions to this localization are described

From the differential diagnostic point of view branchial arteritis is included in the causes of the 'aortic arch syndrome This is a clinical concept applied to the symptomatology found in stenosing processes of one or more of the large branches of the aortic arch, regardless of etiology (MARTORELL & FABRE 1944, FROVIG 1946, ROSS & MCKUSICK 1953) For a differentiation of the various causes of the syndrome roentgenologic examinations may be of help Widened costal grooves have been demonstrated in conventional roentgenograms of the thorax indicating that intercostal arteries serve as collaterals following subclavian artery obstruction (LEVIN & RIGLER 1953, POKER, FINBY & STEINBERG 1958) Osseous anomalies in the area, usually cervical ribs, may be demonstrated An examination with a contrast medium is necessary for a more thorough study of the aortic arch with its branches Thoracic aortography in two cases of branchial arteritis was discussed at some length by WICKBOM 1957

In the present paper we shall discuss the differentiation of disorders which may cause stenosis of the large branches of the aortic arch with special reference to the roentgen diagnosis of branchial arteritis

Material and Methods

The present series comprises 14 cases of aortic arch syndrome including cases not only with multiple but also with solitary stenosis, a progressive arterial disease with multiple stenoses may give rise to signs of impaired circulation of a single artery The clinical aspects of 9 of the cases were discussed by BIRKE, EJRUP & OLHAGEN (1957), and one of them by BIRKE & EKELUND (1959)

Conventional roentgenograms of the thorax were obtained in all cases The arch of the aorta and its main branches were contrast filled in 9 thoracic aortographies after percutaneous catheterization of the right femoral artery

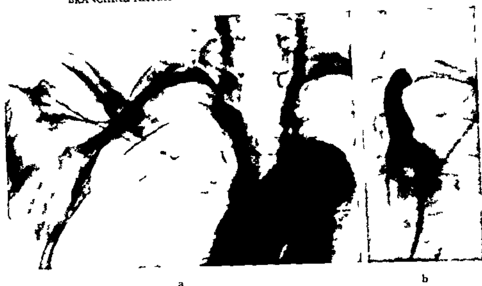


Fig 3 Case 4 Branchial arteritis Thoracic aortography a) Moderately narrowed lumen of summit of right subclavian artery First portion of left subclavian artery poorly filled Smooth contours Left vertebral artery not filled b) Selective arteriography of left subclavian artery at same sitting revealed occlusion at the summit Intercostal collaterals visible

ities nor any elevation of the serum cholesterol values obliteration due to atherosclerosis could therefore reasonably be excluded No clinical or roentgenologic signs of syphilis were evident No other explanation to the symptoms but branchial arteritis could be found

The roentgen findings in the last seven cases were as follows

Case 1 Female aged 23 years (Fig 1) The heart was normal in shape and size Progressive dilatation of the thoracic aorta particularly of the ascending and arch portions was observed over a 7 year period of observation Aortography revealed a thickness of 4 to 5 mm of the upper lateral wall of the distal part of the aortic arch and a slight irregular narrowing about 5 cm in length of the upper portion of the descending aorta The innominate and subclavian arteries had variations in their internal diameters up to the summits where they were occluded The right common carotid artery was occluded after the course of a few centimeters and the left arose abnormally from the innominate artery near the aorta and was markedly narrowed Both vertebral arteries were probably normal their contours were fairly smooth Collateral circulation was provided by local arteries in the vicinity of the occlusions as well as by intercostal arteries

Case 2 Female aged 65 There was relative enlargement of the left ventricle of the heart. The thoracic aorta particularly the ascending portion became progressively dilated during a 7 year period of observation Minute calcium deposits were present in the wall of the arch Aortography (Fig 2) showed twisted main branches The innominate artery had a smooth lumen The right subclavian artery showed moderate narrowings at the summit but its distal part was probably normal in width The axillary artery was considerably narrowed so that its major part and the upper part of the brachial artery had an irregular width of 2 to 4 mm The



Fig 2 Case 2 Branchial arteritis Thoracic aortography Twisted main branches Summit of right subclavian and right axillary and brachial arteries as well as left subclavian and upper part of axillary artery irregularly narrowed remainder of left axillary artery occluded Carotid and vertebral arteries have smooth lumina Collaterals present on both sides

The contrast medium used was a compound of the diatrizoate type (Urografin) For thoracic aortography about 1 ml 60 % medium/kg bodyweight was injected about five centimeters above the aortic ostium For subclavian arteriography 10 to 20 ml and for iliac femoral arteriography 20 to 25 ml 45 % medium were used

No biopsies of the arterial wall were made

Clinical and roentgenologic observations

All 14 patients had signs of impaired vascular circulation of the arms with pain and rapid exhaustion on exercise, particularly with the arms elevated They usually complained of cold hands but none of them presented evidence of Raynaud's phenomenon Oscillography of the arms showed signs of stenosis located centrally in the main arteries Many of the patients suffered from frequent headaches or dizziness, 4 of them had a history of some major neurologic disturbance such as transient hemiparesis, facial paresis, or aphasia In 7 of the patients a systolic murmur was heard over a subclavian or carotid artery All 14 patients obviously had the aortic arch syndrome

Seven of the patients, all females, had the following additional clinical features in common The erythrocyte sedimentation rate was elevated and varied from 30 to 135 mm/hour In the electrophoretic pattern of the serum proteins the gamma globulin was slightly elevated, and there was hypoalbuminemia There were no signs of stenosing processes in the arteries of the lower extrem



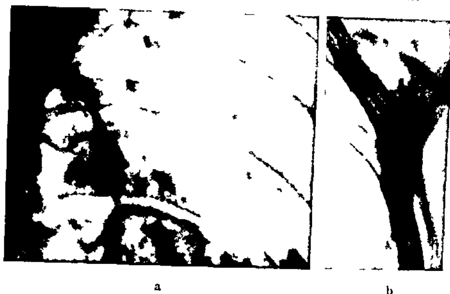
Fig 5 Case 5 Branchial arteritis Arteriography of left axillary and brachial arteries after percutaneous puncture of subclavian artery Smooth narrowing of lumen of axillary artery which is occluded at its junction with the brachial artery Abundant collaterals some of which are narrowed

Case 5 Female aged 34 The heart was normal in shape and size. The thoracic aorta, particularly the ascending portion became progressively dilated during a 3 year period of observation At arteriography (Fig 5) the most distal part of the left subclavian artery and the major part of the axillary artery presented somewhat narrow but smooth lumina The most distal part of the axillary artery and the uppermost part of the brachial artery were completely occluded 3 to 4 cm distal to a cone-shaped narrowing In other parts the brachial artery was rather narrow with slight irregular contours There were abundant collaterals some of which were also narrowed

Case 6 Female aged 62 The left ventricle was relatively enlarged The thoracic aorta was generally widened but without calcifications (one year s observation) At bilateral arteriography the axillary arteries had narrow irregular lumina the narrowings increased at the junction with the brachial arteries where the lumen was about 1 mm The brachial arteries were then occluded for 2 and 4 5 cm respectively distal to which the lumina became smooth Collaterals were present mainly at the level of the occlusions No calcium deposits in the arterial walls of the lower extremities were visible

Case 7 Female aged 43 The heart was normal in shape and size The ascending portion of the thoracic aorta was obviously dilated but without calcium deposits (one year s observation) At aortography and selective arteriography of the left subclavian artery the summit of the vessel was markedly narrowed while the distal part and the axillary artery had long smooth variations in caliber down to half of the normal collaterals had developed at the level of the narrowed summit The first part of the left subclavian artery the innominate artery the right subclavian and the common carotid arteries appeared to be normal

The roentgen findings in the seven cases are summarized in the following Three of the cases had relative enlargement of the left ventricle of the heart, in the remaining four the heart was normal in shape and size



a b

Fig 4 Case 4 (same as in fig 3) Widened left intercostal arteries with notching of ribs b) Distal part of left axillary artery filled by collateral chest wall arteries

left subclavian artery was considerably narrowed at the summit and, still narrowed then continued with slight variations in caliber into the axillary artery after a short distance this vessel was occluded and collaterals had developed The common carotid and vertebral arteries were normal in width The contours in the affected arteries were fairly smooth Arteriography of the distal part of the aorta and the iliac and femoral arteries revealed no signs of atherosclerosis

Case 3 Female aged 39 The heart was normal in shape and size The ascending and arch portions of the thoracic aorta were dilated at 34 years of age At aortography the innominate artery and the subclavian arteries were seen to be moderately and irregularly narrowed particularly on the left side The proximal parts of the axillary arteries were occluded the distal parts and the proximal parts of the brachial arteries being narrowed with fairly smooth contours The common carotid and vertebral arteries seemed to be normal Abundant collaterals along the main stems carried the blood from the aorta to the axillary arteries The collaterals and the axillary arteries distal to the occlusions were filled before and better than the main stems proximal to the occlusions Intercostal and chest wall collaterals were outlined

Case 4 Female aged 47 There was relative enlargement of the left ventricle The thoracic aorta was long and twisted and the ascending and arch portions were dilated (one year s observations) No calcium deposits were visible in the aortic wall At aortography (Figs 3 and 4) the summit of the right subclavian artery was of irregular width the remaining parts of the right subclavian artery the innominate artery and the axillary artery were normal

The left subclavian artery was abruptly occluded at the summit and the flow was not again seen until the midportion of the axillary artery This vessel and the upper part of the brachial artery were narrow Both common carotid arteries and the right vertebral artery were normal the left vertebral artery was not filled The contours were smooth There was a collateral circulation on the left side through local and intercostal arteries primarily the 8th and 9th, and the chest wall arteries The former had caused widening of the costal grooves



Fig 7 Female aged 63 Atherosclerosis Thoracic aortography Twisted main branches Right subclavian and axillary arteries with slightly irregular lumen mostly at the summit same vessels on left side generally more narrowed and slightly irregular again mostly at the summit Metal clips after cervicothoracic sympathectomy to the left

caliber changes of the innominate artery One of the cases also had wall changes in both common carotid arteries, and in a further case there was no filling of one vertebral artery

The narrowings ranged from a slight diminution of caliber to complete occlusion and the variations occurred in different parts of the vessels sections of normal width being seen between the narrowings The contours were completely or fairly smooth and in no case had they the irregularity observed in severe atherosclerosis of the arteries of the lower limb In the case with changes in the carotid arteries the left one also had an anomalous origin from the initial part of the innominate artery When marked narrowings and occlusions were present in the vessels to the upper extremities collaterals had developed, the collaterals were found not only locally but extended through to the intercostal and other thoracic wall arteries A widening of the costal grooves of 8th and 9th left ribs could be demonstrated in one case

Reasonable explanations to the impaired circulation in the arms other than branchial arteritis could be offered in all the remaining 7 patients

The three first two males and one female had either roentgenologic evidence of atherosclerosis or oscillographic signs of stenosing processes in the arteries of the lower limbs or both The two males were 65 and 48 years of age They had no or only slight elevation of the ESR and no changes in the electrophoretic pattern a branchial arteritis did not seem to explain the clinical picture Both had a thoracic aorta that was not dilated although in the elder there were some calcifications in the wall of the arch The beginning of each left subclavian artery was markedly narrowed (Fig 6) while the continuation had slight narrowings The right subclavian artery had in one of the two cases slight changes in its wall while in the second it was



a



b

Fig 6 Male aged 48 Atherosclerosis a) Thoracic aortography Slightly irregular caliber of the right subclavian and axillary arteries Left subclavian and axillary arteries were not filled so well and appear more narrow Intercostal arteries on the same side are better shown b) Arteriography of left subclavian artery Beginning of artery markedly narrowed the continuation presenting a slightly irregular lumen Fairly smooth contours

All the cases had dilation of the whole or part of the thoracic aorta In six cases the ascending aorta and the arch of the aorta were mostly affected and in three cases followed up for from 3 to 7 years this dilation was seen to be progressive One case showed in addition a thickening of the aortic wall and a long moderate narrowing of the uppermost part of the descending aorta The oldest patient had minute calcium deposits in the wall of the aortic arch although no vascular wall changes were demonstrable at lower lumbar aortography and pelvic femoral arteriography In the second oldest patient no calcium deposits were visible in the aorta nor in the vessels of the lower extremities

The large branches of the aortic arch had in all cases narrowings and occlusions situated in the subclavian and axillary brachial arteries, in addition, two had

cervical rib confirmed. In the male the cause of the occlusion was not verified but was probably in the nature of a thoracic outlet disorder with thrombosis of the artery In the fourth case a female aged 58 (Fig 9) the left subclavian axillary and brachial arteries had in general a smaller caliber than those on the right side Narrowings with fairly irregular contours from the subclavian summit to the uppermost part of the brachial artery were observed There was a marked area of narrowing about 1 cm in length, in the distal portion of the axillary artery although a catheter could be passed through it from the brachial artery Many collaterals were demonstrated It was thought that these vascular changes were caused by intimal thickenings and shrinkage of the arterial wall and periarterial tissues after roentgen treatment with high doses to the supraclavian and axillary glands twenty years previously There was also atrophy and teleangiectasis of the skin over the areas of the most marked arterial narrowing The thoracic aorta was moderately dilated which could be explained by the age of the patient. Branchial arteritis was excluded clinically

Differential diagnosis

As the local clinical signs in branchial arteritis are not typical but indicate only the site of the arterial stenosis the differential diagnosis in many cases is difficult The sex and age of the patient the history a careful bedside examination of the peripheral arteries oscillography of the arms and legs and laboratory tests such as the ESR serum protein electrophoresis, Wassermann reaction and serum cholesterol all give valuable clues Conventional as well as contrast medium examinations of the thorax will afford valuable information regarding the site extent and degree of the vascular changes It is our experience that the arterial contrast examination is best done as thoracic aortography after percutaneous catheterization via the femoral artery preferably combined with selective arteriography of the different arteries at the same sitting (cf Fig 3) Direct puncture of the artery proximal to the site of a stenosis (cf Fig 5) may be difficult or impossible The common carotid and the subclavian arteries can, however often be examined after retrograde percutaneous catheterization as puncture is often possible peripheral to a stenosis and even to an occlusion provided sufficient collateral circulation is present the contrast medium may then be forced against the bloodstream by manual injection (cf Fig 9) With most automatic film changers now in use for aortography the dimensions of the films are large enough for demonstrating the arteries at least to the branching of the common carotid arteries and the upper parts of the brachial arteries With regard to the possibilities of surgical therapy in cases with localized vascular changes the demonstration of the common carotid and the lower parts of the vertebral arteries is important

Certain features in conventional films of the thorax may suggest branchial arteritis The dilation of the proximal parts of the aorta is apparently a common finding although previously not reported This change is probably caused by a decreased resistance in the wall due to inflammatory infiltration Its presence in a young female in combination with an unexplained high ESR may suggest the diagnosis and initiate a search for cerebral and ocular disturbances and signs of impaired circulation in the head neck and arms A dilation of mainly



Fig 8

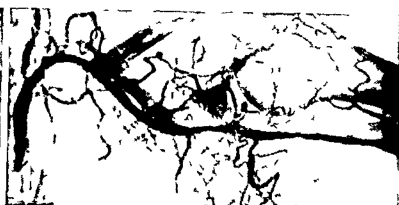


Fig 9

Fig 8 Male aged 39 Probably thoracic outlet disorder Retrograde arteriography of right innominate artery via catheter after percutaneous puncture of common carotid artery (compressed during the injection of contrast medium) Occlusion of subclavian artery probably due to thrombosis Normal smooth lumina of innominate and common carotid arteries

Fig 9 Female aged 58 Arterial stenosis after extensive roentgen therapy Arteriography of left subclavian axillary and brachial arteries after percutaneous catheterization of brachial artery the arteries are narrowed and vary in caliber Markedly narrowed region 1 cm in length present in axillary artery Collaterals present

normal in appearance The younger patient had extensive mainly intimal calcifications of the walls of the arteries of the pelvis and the lower extremities and right femoral arteriography revealed narrowings of the vessel The female 63 years of age had an elevated ESR the electrophoretic pattern was only slightly altered Branchial arteritis could thus not be excluded but the obvious atherosclerosis and repeated respiratory and bladder infections could explain the clinical picture The case was therefore not placed among those of branchial arteritis The patient had a dilated thoracic aorta with calcium deposits and twisted main branches and narrowings of both subclavian and axillary arteries particularly on the left side (Fig 7) In the arteries of the lower extremities extensive atherosclerotic changes with calcifications and narrowings were seen at arteriography

None of these 3 cases revealed wall changes of the common carotid arteries It may be noted that the contours of the affected subclavian and axillary arteries had not the high degree of irregularity which is often seen in atherosclerosis of the femoral arteries

In the remaining 4 cases one a female aged 44 had a fusiformly dilated thoracic portion and very extensive medial calcifications in the entire thoracic and upper abdominal portions of the aorta The etiology was obscure the roentgenologic suggestion of syphilis could not be confirmed clinically However the heart was enlarged and in both supraclavicular regions apparently dilated heavily pulsating subclavian arteries were palpated and loud murmurs heard Retrograde right brachial arteriography revealed occlusions in the axillary and brachial arteries which were otherwise unchanged collaterals were present The occlusions were possibly due to embolism emanating from an aneurysm in the thoracic outlet A male aged 39, had an occlusion of the right subclavian artery (Fig 8) and a female aged 38 an occlusion of the distal part of the right axillary artery Variations in caliber of the distal part of the subclavian artery were also evident in the latter and in addition a cervical rib was present on the same side collaterals had developed The two last mentioned cases had a normal ESR and in neither of them were any changes revealed in other contrast filled arteries nor was any dilation of the aorta found The female was operated upon twice and the arterial wall changes and the

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the ascending aorta is found also in congenital heart and vessel failures, such as constriction of the aorta and persistent ductus arteriosus. In the majority of these cases the clinical findings and angiocardiograms give a definite diagnosis. If rib notching indicating dilated intercostal arteries is present, constriction of the aorta must be excluded before a stenosing process in the subclavian artery is indicated. It will also be noted that the hereditary disorder of connective tissue, called Marfan's syndrome, may cause progressive dilation of the thoracic aorta. The disease starts in youth, and pregnancy is said to accelerate the dilation. However, this condition is combined with insufficiency of the aortic ostium and enlargement of the left ventricle. A chronic dissecting hematoma (aneurysm) in the aorta is a frequent complication. In the same way, the fusiform aneurysmal widening of the thoracic aorta in syphilis is most often combined with aortic insufficiency and an increase in heart size. The post-stenotic dilation in valvular aortic stenosis, and the dilation of the thoracic aorta in hypertension and arteriosclerosis may also be excluded with the help of other clinical and roentgenologic signs.

In addition to dilation of the ascending portion of the aorta and extensive and marked changes in the branchial branches, one of the cases listed as branchial arteritis (cf. Fig. 1) also had thickening of the aortic wall and narrowing of the descending aorta. It seems reasonable to presume that these changes also were caused by the same inflammatory infiltration.

When at contrast medium examination narrowings and occlusions of the branchial arteries are present a roentgenologic diagnosis may again be suggested. However, the findings must be correlated to arteriographic features in other areas as well as to clinical signs.

Congenital vascular anomalies primarily include variations in the origin of the main branches of the aortic arch (cf. Fig. 1), but rarely variations in caliber. Narrowing of the origin of the left subclavian artery may appear when the vessel is in any way involved in a coarctation of the aorta. Congenital anomalies should therefore not be difficult to distinguish from branchial arteritis. On the other hand, abnormal arteries more often than normal ones may be affected by disease.

Other conditions with panarteritis of unknown etiology are thromboangitis obliterans, polyarteritis nodosa, and temporal arteritis. The inflammatory lesions in the first condition involve chiefly medium sized and small arteries. The distal parts of the extremities, primarily the lower limbs, are involved. Thromboangitis obliterans is a disease which occurs almost exclusively in men under 40 years of age, and is most commonly associated with a superficial phlebitis of the smaller veins. In the case of polyarteritis nodosa mostly minute vessels are affected. There are widely disseminated changes in almost any organ and tissue in the body and this suggests a diffuse systemic process, involving particularly the kidneys, gastrointestinal tract, and peripheral nerves. The incidence among males is greater than among females. Both diseases have

a characteristic histologic picture Branchial arteritis is distinguished from them by its localization sex distribution, and absence of thrombophlebitis Temporal arteritis although usually situated in branches of the external carotid arteries, may occasionally involve the aortic arch and its main branches, as well as other large or medium sized arteries (CARDELL & HANLEY 1951) The two disorders may therefore have local features in common However, temporal arteritis is characterized by an acute subacute and branchial arteritis by a chronic course usually for years This difference is reflected in the serum protein pattern the gamma globulin elevation found in branchial arteritis not being present in temporal arteritis Sex and age distributions are also different temporal arteritis mostly affecting the elderly men and women equally

Another condition that may cause arterial occlusion is syphilis However, this disease usually presents typical serum reactions Furthermore syphilitic infiltration of the walls of the branchial arteries is very rare and, if present is part of an aortitis giving clinical signs of aortic insufficiency Involvement of the arteries is also a late manifestation of syphilis The origin of the branches may be occluded by changes in the aortic wall or by emboli arising from a thrombosed aneurysm In the presence of an aneurysm conventional roentgenograms may demonstrate the deformity of the thoracic aorta, and aortography will give further information as to the site and size of the aneurysm One should also bear in mind that syphilitic aortitis predisposes to the development of arteriosclerosis with local calcium deposits

Atherosclerosis obliterans in distinction to branchial arteritis primarily affects the arteries of the lower extremity in subjects of middle or old age The frequency of atherosclerosis of the branchial branches of the aorta is unfortunately not exactly known Extensive atherosclerosis of the legs in an elderly subject should suggest changes in the upper aortic branches of a similar nature, at least if the patient has no unexplainable ESR elevation and a normal gamma globulin value However atherosclerosis of the larger arteries of the upper extremity must be very uncommon as compared with the lower extremity because arterial calcifications in this region are very rarely seen in conventional films of the thorax or in soft tissue films of the upper arms When present atherosclerosis seems to have a predilection for the root of the left subclavian artery (ALLEN BARKER & HINES 1955) which is in agreement with the findings in two of our cases (cf Fig 6) In the present atherosclerotic cases the variations in the lumen had fairly smooth contours, and in this respect there was no difference between the atherosclerotic and branchial arteritic cases

Pseudoxanthoma elasticum is also discussed as a differential diagnostic possibility (BIRKE et coll 1957) This is a systemic disease of the elastic tissue with typical cutaneous and vascular lesions Arterial occlusion in the lower extremities appears at an early age This also occurs in the upper extremities but this location does not seem to be as common (CARLBORG et coll 1959)

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subclavian arteries should never be omitted and any murmur detected should be differentiated from one of cardiac origin

To sum up the interpretation of the dilation of the thoracic aorta in conventional films and of narrowings, occlusions and collateral circulations in aortograms or arteriograms in branchial arteritis should not be difficult It is much easier to establish the changes than to determine their nature The exclusion of other conditions and the true diagnosis may not be possible until both the roentgenographic and clinical findings are in acceptable agreement

SUMMARY

The roentgen and differential diagnoses are discussed in a series of 14 cases of stenosis of the large branches of the aortic arch including 7 cases with signs of branchial arteritis The difficulty in separating the vascular changes in branchial arteritis from other vascular lesions giving rise to the aortic arch syndrome particularly atherosclerosis obliterans is stressed

ZUSAMMENFASSUNG

Die Rontgendiagnose und die Differentialdiagnostik werden in eine Serie von 14 Fallen mit Stenose der grossen Zweige des Aortabogens diskutiert das Material enthalt 7 Falle die Symptome einer branchialen Arteritis zeigten Die Schwierigkeit die Gefassveranderungen bei branchialer Arteritis von anderen Gefass eranderungen abzugrenzen welche Anlass zum Aortabogensyndrom geben insbesondere der Arterioskllerosis obliterans wird betont

RÉSUME

Se fondant sur une série de 14 cas de stenose des grosses branches de la crosse de l aorte dont 7 cas présentaient aussi des signes d artérite branchiale les auteurs étudient le diagnostic radiologique et différentiel de cette affection Ils insistent sur la difficulté qu il y a pour distinguer les altérations vasculaires de l artérite branchiale d autres lésions vasculaires donnant un syndrome de la crosse aortique en particulier l athéro clerose oblitérante

REFERENCES

ALLEN E V BARKER N W and HINES JR E A Peripheral vascular diseases 2nd ed W B Saunders Philadelphia and London 1955

ASK UPMARK E On the pulseless disease outside of Japan Acta med scand 149 (1954) 161

— and FAJERS C M Further observations on Takayashu s syndrome Acta med scand 155 (1956) 275

BIRKE G EJRUP B and OLHAGEN B Pulseless disease Angiology 8 (1957) 433

— and EKELUND L G Pulseless disease (Takayashu s syndrome) (In Swedish) Nord med 62 (1959) 1120

CARDELL, B S and HANLEY T Fatal case of giant cell or temporal arteritis J Path Bact 65 (1951) 587

CARLBORG U EJRUP B GRONBLAD E and LUND F Vascular studies in pseudoxanthoma elasticum and angioid streaks Acta med scand (1959) Suppl 350

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In a case examined by us and reported by BIRKE et coll and CARLBORG et coll there were arterial occlusions in the forearm, hand and thigh, but no changes in the brachial and axillary arteries were present

Arterial embolism is almost always associated with advanced heart disease particularly with auricular fibrillation The signs of an embolus in the great majority of cases appear suddenly but it is worth noting that they may take several hours to develop

The shoulder girdle compression syndrome, and the thoracic outlet syndrome are most often combinations of signs referable to the brachial plexus and subclavian vessels, mostly in females The first syndrome includes cases with normal anatomic thoracic outlets, but the relationship of the structures changes with altered position The second syndrome includes cases with anatomic abnormalities of the thoracic outlet In both cases compression of nerves and vessels may appear In the majority of cases the neurologic signs predominate and the vascular signs are minimal When the compression of the arteries is prolonged, the vascular walls are damaged, which leads ultimately to occlusion by thrombosis Emboli may be thrown off from the thrombus to a more distal part of the artery A careful examination of the arterial pulsations in different positions of the head and arms, and roentgenologic demonstration of anatomic abnormalities such as cervical ribs, may help in the differential diagnosis of the vascular changes as in one of our cases Arteriography may demonstrate the local stenosis or occlusion, and there may be distal occlusions due to emboli Other arteries are not involved, in distinction to branchial arteritis, and are therefore not narrowed

Tumours in the upper mediastinum may displace the actual vessels However, pulse changes due to their expansion seem to be rare (ROSS & MCKUSICK 1953)

As a last differential diagnostic possibility changes in the walls of the vessels secondary to radiation will be noted GOTTLOB (1952) has reported one case with narrowings of the pelvic arteries after radiotherapy, postmortem examination revealed perivascular fibrosis and shrinkage It seems reasonable to presume that similar wall changes were present in our patient

It is noteworthy in the present series of branchial arteritis that the lesion was, with one exception, restricted to the thoracic aorta and to the subclavian and axillary arteries This might be due to the fact that no neurologic clinic is served by our roentgen department, and patients with carotid stenosis will probably collect in such clinics However, it may also possibly indicate that limitation of the disease to the subclavian area is more common than is believed The arm symptoms are in general milder and less troublesome than the cerebral ones and this may explain why the condition when restricted to the subclavian areas may fail to be recognised until there is greater awareness of the entity This possibility should therefore be kept in mind when investigating patients with an unexplained elevated ESR, even when no clinical signs of impaired cerebral or ocular circulation are found Auscultation of stenosed carotid and

subclavian arteries should never be omitted, and any murmur detected should be differentiated from one of cardiac origin

To sum up, the interpretation of the dilation of the thoracic aorta in conventional films and of narrowings occlusions and collateral circulations in aortograms or arteriograms in branchial arteritis should not be difficult It is much easier to establish the changes than to determine their nature The exclusion of other conditions and the true diagnosis may not be possible until both the roentgenographic and clinical findings are in acceptable agreement

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REFERENCES

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BIRKE G EJRUP B and OLHAGEN B Pulseless disease Angiology 8 (1957) 433

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FROVIG A G Bilateral obliteration of the common carotid artery Acta psychiat scand (1946) Suppl 39

GOTTLOB, R Über Strahlenschaden der grossen Blutgefässe Wien klin Wschr 64 (1952) 361

KOSZEWSKI B J Branchial arteritis or aortic arch arteritis A new inflammatory arterial disease (pulseless disease) Angiology 9 (1958), 180

LEVIN B and RIGLER, L G Rib notching following subclavian artery obstruction Radiology 62 (1954), 660

MARTORELL I and FABRÉ, T J El sindrome de obliteracion de los troncos supraaorticos Med clin (Barcelona) 26 (1944) 17

ÖDMAN P Percutaneous selective angiography of the main branches of the aorta Acta radiol 45 (1956), 1

— Thoracic aortography by means of a radiopaque polythene catheter inserted percutaneously Acta radiol 45 (1956), 117

POKER N LINBY N and STEINBERG, I The subclavian arteries roentgen study in health and disease Amer J Roentgenol 80 (1958), 193

ROSS R S and McKUSICK V A Aortic arch syndromes Arch intern med 92 (1953) 701

SAVORY, W S Case of a young woman in whom the main arteries of both upper extremities and of the left side of the neck were throughout completely obliterated Med chir Trans 39 (1856) 205

SELDINGER, S I Catheter replacement of the needle in percutaneous arteriography Acta radiol 39 (1953) 281

TAKAYASHU, M quoted by ASK UPMARK and by KOSZEWSKI

WICKBOM I Arteriography in brachiocephalic arteritis (pulseless disease or the Takayashu syndrome) Acta radiol 48 (1957), 321

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SYMETRIE DU CRANE NORMAL CHEZ LES ADOLESCENTS ET LES ADULTES

par

ANDRE THIBAUT

Sur les cliches d examens complets et faits avec soin il est generalement facile de reconnaitre les asymetries importantes qu il s agisse d une hypo plasie de la moitie du crane comme on peut l observer dans des cas d atrophie hemispherique infantile (DAVIDOFF MASSON ROSS) par exemple ou d un ballonnement plus ou moins important localise comme dans beaucoup d hy dromes unilateraux (DAVIDOFF, DYKE BULL)

Des difficultés surgissent quand il s agit de reconnaitre une asymetrie peu importante et de definir si elle est ou non pathologique Ce probleme de la limite du normal et du pathologique s est toujours pose au radiologue quelle que soit la region exploree Ce travail a pour but d apporter une contribution dans ce domaine en ce qui concerne la morphologie du crane normal

Analyse de la litterature Nous savons par les anatomistes qu une symétrie parfaite du crane n existe que chez 10 a 12 % des individus de l espece humaine Cette constatation est basée sur des mensurations de cranes secs (LEBON) C'est elle qui a conduit TALAIRACH a negliger les points de reperes craniens osseux dans ses études stereotaxiques des formations nerveuses sous corticales

Soumis à la Rédaction le 9 Septembre 1960

Au point de vue radiologique Lefevre, Guy & Metzger ont étudié la symétrie du crane chez plusieurs centaines d'enfants normaux et MacRae chez 56 sujets atteints d'épilepsie non tumorale où l'encéphalographie fractionnée avait montré des signes d'atrophie cérébrale ou corticale de siège et d'étendue variables. Pour leur étude, ces auteurs ont calqué les contours du crane examiné de face en incidence postéro antérieure demi axiale et accessoirement en position antéro postérieure demi-axiale et axiale. Sur les calques, ils tracent la ligne médiane qu'ils définissent par deux points qui sont le milieu de la gouttière du sinus longitudinal supérieur et le milieu du dos de la selle pour MacRae, et pour les trois premiers auteurs, le nasion ou l'apophyse odontoïde avec, soit le milieu de la gouttière du sinus longitudinal supérieur, ou le milieu de la suture interpariétale. Ensuite, ils mesurent comparativement le diamètre transversal des deux moitiés du crane sans préciser toutefois quel point de la voute ils choisissent.

Lefevre, Guy & Metzger ne rapportent pas les détails de leurs observations. Ils concluent à l'existence d'une asymétrie *physiologique chez l'enfant* normal mais sans en décrire les caractères différentiels d'une asymétrie pathologique. D'ailleurs, ils ne définissent pas ce qu'ils entendent par l'enfant normal.

Quant à MacRae, il trouve une asymétrie chez 50 % de ses malades et en fait un signe important dans le tableau radiologique de l'épilepsie non tumorale. L'asymétrie est légère quand elle dépasse 2 mm, modérée quand elle est comprise entre 2 et 5 mm et importante quand elle dépasse 5 mm. Cependant l'auteur ne spécifie pas les caractéristiques techniques de l'appareillage utilisé pour ces examens. Chez ces mêmes malades il a recherché d'autres manifestations d'asymétrie cranienne, dont le développement inégal des sinus frontaux et des mastoïdes, et aussi le décalage éventuel du bord supérieur des rochers dans le plan vertico frontal. De l'analyse de ces signes, il résulte que le tableau de l'hypoplasie d'une moitié du crane comme on le voit dans l'hémi atrophie cérébrale ne fut qu'exceptionnellement présent. Et pourtant l'auteur ne semble pas faire de distinction entre asymétries et hypoplasies puisqu'en donnant le pourcentage de celles ci, il cite le pourcentage de celles là.

La question de savoir s'il y a une différence entre les asymétries 'physiologiques' de Lefevre, Guy & Metzger et les asymétries 'pathologiques' de MacRae, ne nous paraît pas pouvoir être résolue, faute de définition du sujet normal et d'étude de contrôle chez de pareils sujets. D'ailleurs, la méthode de mensuration utilisée par tous ces auteurs n'est pas satisfaisante. Parce qu'elle est liée au caractère de l'image radiographique, l'appréciation d'une asymétrie est délicate. La moindre rotation de la tête dans les projections de face, détermine une fausse asymétrie. Il en résulte que tous les examens ne se prêtent pas à des mensurations.

Pour que la projection soit bonne, il faut que le rayon principal soit compris dans le plan médian sagittal et que celui ci soit perpendiculaire au plan du film. Mais la difficulté est de matérialiser de façon précise le plan médian

sagittal sur le crane a radiographier Beaucoup de methodes ont eté preconisees (PORCHER LEDOUX LEBAR, OLSSON) Cependant, quel que soit l artifice utilise, c est finalement sur le film que l on peut juger de la perfection de la position de la tete et du centrage

Si le rayon principal perpendiculaire au plan du film, est effectivement compris dans le plan median sagittal du crane, tous les points médians reperes sur le cliche peuvent etre reunis l un a l autre et se trouvent sur une meme droite Si une droite definie par deux d entre eux passe par un troisieme, la projection est parfaite JACKSON utilise le lambda, le bregma et le nasion Ces trois points sont parmi les points medians decrits par les anthropologistes (BROCA), malheureusement ils ne sont pas toujours reperables en ce qui concerne le lambda et le bregma tandis que le nasion est tres difficile a identifier sur les cliches de face

JACKSON considere les mensurations inutiles ou peu utiles pour distinguer les asymetries normales des asymetries pathologiques Il signale que les asymétries pathologiques se manifestent non seulement par des modifications de volume mais aussi par d autres signes morphologiques qui permettent bien souvent de prejuger de leur cause etant donne nos connaissances sur la croissance des os du crane et leurs reactions aux agents mécaniques Cette opinion est basee sur ses propres observations de plusieurs cas d asymetrie pathologique de nature differente et sur les travaux d autres auteurs dont CHILDE BULL, HARDMAN & JUPE

Ces autres signes morphologiques consistent en modifications de l epaisseur de la voute du relief de la theque interne de la pneumatisation des cavités sinusales paranasales et des mastoides

Cependant LOMBARDI a rapporte l observation d un cas ou l encéphalographie fractionnee et l artériographie carotidienne furent normales alors que l examen direct avait montre une asymetrie du crane associee a d autres signes morphologiques realisant un tableau semblable a celui rencontre dans certains hydromes ou hematomes sous duraux chroniques juveniles (BULL THIBAUT)

Cette observation a un grand intéret Elle permet de penser (en dehors d autres hypotheses par exemple une fausse asymetrie) que l association de modifications morphologiques convergentes ne suffit pas pour donner un caractere pathologique a une asymetrie du crane et qu un facteur quantitatif caractérisant aussi bien l importance de l asymetrie que celle des modifications morphologiques associees peut constituer un elément determinant dans le diagnostic differentiel

Materiel Nous considerons qu une asymetrie pathologique traduit par définition une modification du contenu de la boite cranienne Des lors nous avons retenu comme critere du crane normal l integrité anatomique macroscopique de son contenu

C est donc sur une base anatomique que nous avons selectionne notre ma

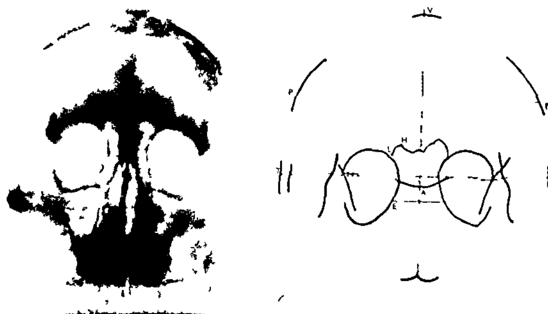


Fig 1 Repères utilisés pour les mensurations en incidence postero antérieure demi axiale

A — Point d intersection de la ligne de l étage antérieur avec la ligne mediane
V — Point le plus haut du contour externe de la voute sur la ligne mediane
O — Point d intersection de la ligne de la grande aile du sphenoide avec le contour interne de la paroi supéro externe de l orbite
P — Point du contour externe de la voute situé sur la perpendiculaire elevée de la ligne mediane en un point situé à mi-distance entre A et V
T — Point du contour externe de la voute situé sur une perpendiculaire à la ligne médiane passant à hauteur des points 0 (bien souvent ces deux points ne sont pas à la même hauteur dans ce cas la perpendiculaire passe entre les deux)
H — Point le plus elevé du sinus frontal
L — Point le plus externe du sinus frontal
E — Point du contour externe de l ethmoide situé sur une perpendiculaire élevée de la ligne médiane 10 mm en dessous du point A

teriel en postulant que l'A ou l'encéphalographie fractionnée avait ete négative, c'est a dire avait montre l absence de tout deplacement, deformation ou dilatation du systeme ventriculaire et des espaces sous arachnoidiens, le contenu du crane etait normal Cependant, comme ce travail a ete entrepris aussi pour servir de base a l étude de la symétrie du crane dans l epilepsie non tumorale (Ruggiero, Thibaut, Hecaen & Dell 1960) nous n avons retenu dans notre materiel que les malades non épileptiques Leur age varie entre 15 et 50 ans

Cent examens ont eté etudiés Tous avaient été jugés suffisants pour les besoins cliniques et considérés comme négatifs avec l optique de routine habituelle

Chaque examen comporte au *moins quatre incidences profil*, face postéro antérieure demi axiale, antéro postérieure demi axiale et axiale

Tous ont ete realise au craniographe de Lysholm, avec un foyer d une surface de 2 mm/2 mm et a la distance focale de 70 cm

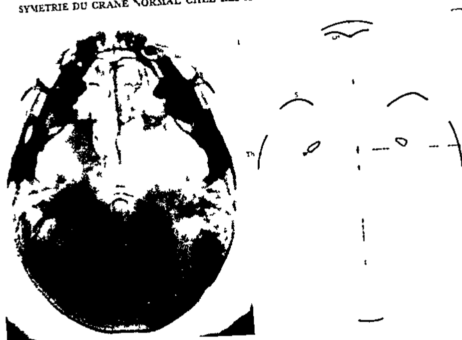


Fig 2 Reperes utilises pour les mensurations en incidence axiale

S — Point le plus anter eur du contour anterieur de la grand aile du sphénoide
Th — Point du contour externe de la oute situe ur une perpendicula re à la ligne mediane passant à hauteur des trous p tits ronds
Df — Point situ sur le contour po t rieur du s nus frontal 10 mm en dehors de la ligne mediane

Pour chaque cas nous avons revu les clichés en projection axiale et postero anterieure demi axiale en vue de mensurations et recherche sur les quatre cliches de chaque examen l existence eventuelle de petits signes de developpement asymetrique de caractere plus morphologique que volumetrique

Technique de mensurations Nous avons utilise un negatoscope a lumiere tres intense de maniere a bien distinguer les contours osseux et un papier transparent millimetré que nous avons applique et fixe sur les cliches a l aide de pinces métalliques

Les points medians que nous avons choisis sont le bregma le lambda la base de la cloison mediane du nez le milieu du nasion, la faux ou l epiphyse calcifiée et sur la suture interparietale un point quelconque situé sur un segment de droite reunissant les points d inversion de la courbe sinusoide dessinee par les incisures de la suture Tous les cliches ou trois de ces points n ont pu etre reperés et ceux ou reperés et reunis trois points medians ne se trouvaient pas sur une meme droite ont ete eliminés

Tableau 1

Caractères des asymétries unilatérales observées sur l'incidence postéro antérieure demi axiale

Nombre de cas selon le siège et le coté de la réduction transversale					Nombre des cas où l'épaisseur de la voute est plus grande égale ou moindre du coté réduit par rapport à l'autre			Nombre de cas où le développement des sinus est plus marqué égal ou moindre du coté réduit par rapport à l'autre					
								Sinus frontaux			Sinus ethmoïdaux		
Siège			G	D	+	=	—	+	=	—	+	=	—
Réduction d'un diamètre seulement		17											
P	9		6	3	2	4	3	1	4	4	7	0	2
T	8		5	3	1	3	4	3	3	2	2	3	3
Réduction des deux diamètres (P et T)		42	18	24	6	24	12	7	21	14	15	6	21
Total		59	29	30	9	31	19	11	28	20	24	9	26

Dans les 100 cas, 68 avaient un cliché en incidence de face postéro antérieure demi axiale mesurable, 68 un cliché en incidence axiale et 50 des clichés mesurables dans les deux incidences.

Sur le papier calque, nous avons tracé la ligne médiane, ainsi qu'un certain nombre de points choisis arbitrairement pour nos mesures (Figs 1 et 2). Nous avons mesuré la distance séparant les points P, T, et Th de la ligne médiane et nous avons calculé la différence d'un coté par rapport à l'autre. En P, le diamètre transversal correspond à celui de la région pariétale, en T et Th, de deux régions différentes de la fosse temporale. En ce qui concerne les points S, nous avons mesuré leur décalage dans le plan horizontal. Ce décalage indique que la grande aile du sphénoïde est plus saillante vers l'avant d'un coté sans traduire nécessairement une différence de diamètre antéro postérieur des fosses temporales, mais quand il coïncide avec une différence dans le même sens d'un ou des deux diamètres transversaux de la région temporale, nous avons admis que les fosses temporales étaient asymétriques. Ensuite, nous avons mesuré l'épaisseur de la voute à hauteur du point T et calculé les différences des deux cotés.

Enfin, par les mesures des écarts entre les points H, L, Df et L, nous avons voulu objectiver les asymétries de développement des cavités sinusales paranasales. Cette méthode est évidemment imprécise mais schématise les éléments sur lesquels nous nous basons pour dire qu'un sinus est plus développé d'un coté que de l'autre. Elle n'est pas appliquée pour comparer le développement des apophyses mastoïdes que nous avons étudié à part avec d'autres aspects morphologiques que peuvent revêtir les asymétries du crane.

Tableau 2

Caractères des asymétries unilatérales observées sur l'incidence axiale

	Nombre de cas selon le siège et le coté de la réduction			Nombre de cas où la profondeur du sinus frontal est plus grande, égale ou moindre du coté réduit par rapport à l'autre		
Siège		G	D	+	=	—
Réduction isolée du diametre Th	8	6	2	6	2	0
Existence isolee d'un décalage postérieur de S	10	7	3	5	3	2
Association d'une réduction du diametre Th et d'un décalage postérieur de S	34	23	11	11	8	15
Total	52	36	16	22	13	17

Les asymetries observees sur l'incidence de face postero anterieure demi axiale. Sur les 68 examens les diametres transversaux sont symetriques dans 3 cas. Dans les 65 autres cas une asymetrie transversale est presente. Elle est de type alterne dans 6 cas, c'est a dire que le diametre temporal est réduit d'un coté et le diametre pariétal du cote opposé. Enfin dans les 59 cas restants l'asymetrie est unilaterale, portant sur un ou les deux diametres à la fois, nous en avons rapporté les caracteres dans le Tableau 1.

Les asymetries observees sur l'incidence axiale. Sur les 68 examens dans 5 cas les points Th et S sont symetriques. Dans les 63 autres cas, il existe une asymetrie. Dans 11 cas elle est de type alterne, le diametre transversal étant reduit d'un coté tandis que de l'autre cote la grande aile du sphenoide est moins saillante vers l'avant. Enfin dans les 52 cas restants, l'asymetrie est unilaterale et se manifeste soit par l'existence isolee d'une reduction du diametre transversal ou d'une saillie moins marquee vers l'avant de la grande aile du sphenoide, soit par l'association de ces deux signes, nous en avons rapporte les caractères dans le Tableau 2.

La frequence des asymetries par ordre de grandeur croissante (Tableau 3). Dans les conditions techniques que nous avons definies plus haut, les differences de diametres sont inferieures à 3 mm dans 58 % des cas, elles *ne depassent pas* 5 mm dans 95 % des cas et ne sont jamais superieures a 8 mm.

Resultats des mensurations

Les caracteres des asymetries dans les 50 cas dont les deux incidences avaient pu etre mesurees. Nous avons confronté les resultats des mensurations pratiquées sur chaque incidence. Une symétrie transversale vérifiee sur les deux incidences

Tableau 3

Ordre de grandeur des asymétries mesurées sur les deux incidences

Siège	Total	Nombre de cas par différence de grandeur croissante (en mm)				
		1 à 3	3 à 6	6 à 9	9 à 16	16 et +
Diamètres transversaux						
P	57	35	19	3	0	0
T	55	30	23	2	0	0
Th	56	32	19	5	0	0
Décalage des points S	55	34	20	1	0	0
Épaisseur de la voûte	32	30	2	0	0	0
Largeur du massif ethmoïdal	53	40	13	0	0	0
Sinus frontaux						
profondeur	50	45	4	1	0	0
hauteur	64	36		23	3	2
largeur	60	36		21	2	1

n'existe dans aucun cas. 28 cas c'est à dire 56 % des sujets ont une asymétrie non systématisée dans 17 cas, l'asymétrie est unilatérale sur chaque incidence mais les cotés ne concordent pas, dans les 11 autres cas, l'asymétrie est alterne sur une incidence et unilatérale sur l'autre (7 fois l'asymétrie est unilatérale sur l'incidence postéro antérieure demi axiale et 4 fois sur l'incidence axiale) 22 cas, c'est à dire 44 % des sujets, ont une asymétrie unilatérale de siège variable (Tableau 4). Dans 7 cas elle n'est démontrée que par une seule incidence tandis que dans les 15 autres elle se vérifie sur les deux incidences. Dans 16 % des cas elle intéresse tous les diamètres de telle manière que toute une moitié du crâne est plus petite que l'autre mais dans aucun de ces cas une voûte plus épaisse et un développement plus important des sinus ne coïncident du coté où les diamètres sont réduits. 50 % des cas ont une asymétrie des fosses temporales, la voute n'est jamais plus mince du coté où la fosse temporale est plus grande (Tableau 5).

Pour rechercher une prédominance éventuelle de coté, nous avons classé les asymétries unilatérales en deux groupes suivant le coté réduit. La répartition se fait en nombre sensiblement égal à gauche et à droite dans l'incidence postéro antérieure demi axiale (Tableau 1) tandis que dans l'incidence axiale le coté gauche est réduit dans 69 % des cas (Tableau 2). Dans les 22 cas où l'examen du crâne était mesurable sur les deux incidences, c'est le coté gauche qui est réduit chez plus de 68 % des individus (Tableau 4), cependant, dans les 11 cas où l'asymétrie porte sur les fosses temporales, il n'y a plus aucun indice de dominance (Tableau 5) le coté droit étant plus petit chez 6 individus et le coté gauche chez les 5 autres.

Enfin, pour mettre en évidence un corrélation possible entre les asymétries

Tableau 4

Caractères des asymétries unilatérales observées chez les sujets dont les deux incidences étaient mesurables Comparaison a e les variations du volume normal des ventricules lateraux

Siege et coté de la reduction		Épaisseur de la voute plus grande égale ou moindre du coté reduit par rapport à l autre					Developpement des sinus plus marqué egal ou moindre du coté reduit par rapport à l autre						Volume des ventricules lateraux		
							S nus frontaux			Sinus éthmoidaux			Égal	Asymétrique (Coté du ventricule + gros)	
No des cas	Siège	G	D	+	=	—	+	=	—	+	=	—		G	D
19	P T Th, S	+				+	+			+				+	
54	—		+		+				+	+			+		
77	—		+			+	+			+				+	
12	P T Th	+				+	+					+	+		
13	—	+			+				+	+			+		
28	—		+		+				+	+				+	
83	—		+			+	+					+	+		
10	P T S	+			+				+	+			+		
21	—	+			+		+			+				+	
81	P S	+		+			+					+	+		
3	P Th S	+		+			+					+		+	
5	—	+		+			+					+		+	
24		+				+			+			+	+		
27	T Th S		+			+			+			+	+		
29	T S		+		+		+					+		+	
18	T P	+		+			+				+			+	
26	—	+			+		+			+				+	
32	—	+		+			+					+	+		
66	P	+		+					+	+					
86	T	+			+		+				+		+		+
2	Th S	+			+			+			+		+		
6	—		+		+		+					+		+	
		15	7	6	10	6	14	1	7	9	3	10	11	10	1

ventriculaires physiologiques (LINDGREN, RUGGIERO) et les asymetries craniennes normales nous avons mis en parallele les unes et le autres chez les 22 sujets ou nos mensurations avaient démontre une asymetrie cranienne unilaterale controlée sur les deux incidences Alors que les diametres craniens sont reduits a gauche dans 69 % des cas et à droite dans 31 %, les ventricules lateraux eux sont symetriques dans 50 % des cas Si le ventricule lateral gauche est

Tableau 5

Caracteres des asymétries des fosses temporales dans les cas d asymétries unilatérales observées chez les sujets dont les deux incidences étaient mesurables

No	Siege de l asymétrie	Coté augmente		Épaisseur de la voute moindre égale ou supérieure du coté plus grand par rapport à l autre coté		
		D	G	+	=	—
19	T, Th S	+		+		
54	—		+		+	
77	—		+	+		
27	—		+	+		
12	T, TH	+		+		
13	—	+			+	
28	—		+		+	
83	—		+	+		
29	T S		+		+	
10	—	+			+	
21	—	+			+	
Total 11		5	6	5	6	0

plus gros que le droit dans 40 % des cas ou le cote gauche du crane est réduit, le ventricule droit n est jamais plus gros que le gauche dans les cas ou c'est le cote droit du crane qui est reduit (Tableau 4)

Variations morphologiques

Rochers Les principales anomalies decrites au niveau des rochers dans les asymetries craniennes pathologiques consistent essentiellement en pneumatisation du bord postéro-superieur de l os et decalage en hauteur ou obliquité plus importante de son grand axe Ces anomalies sont decelables sur les cliches de face postero anterieure demi axiale Nous les avons recherchees dans nos 68 cas mesurables sur cette incidence Dans aucun cas nous n'avons observé de pneumatisation unilaterale du bord postéro superieur mais dans 20 cas il y avait un leger decalage des axes en hauteur, 11 fois le droit etait plus haut que le gauche et 9 fois le gauche plus haut que le droit Parmi ces 20 cas, 4 avaient une reduction des diametres transversaux de la fosse temporale d un coté et tous les 4 du cote gauche, dans un cas le rocher droit etait legerement décalé vers le haut et le gauche dans les trois autres

Mastoides Dans 2 cas sur les 100, il y avait une asymétrie nette de developpement des mastoides et dans un de ces cas le crane avait ses diametres réduits du cote opposé

Theque interne Le relief de la theque interne avait un aspect et une importance extremement variable d'un sujet a l'autre mais dans aucun cas nous n avons observe d'asymetrie nette

Petites ailes du sphénoïde Dans tous les cas les petites ailes du sphénoïde avaient une morphologie normale et ne presentaient pas de decalage en hauteur

Conclusion

1 Nous avons postule que l asymetrie pathologique traduisait par défini tion une modification du contenu cranien. Nous avons *défini comme crane normal* le crane dont le contenu macroscopique était normal, c'est à dire ou l encéphalographie fractionnee n avait montre ni deplacement ni deformation ni dilatation du systeme ventriculaire et des espaces sous arachnoïdiens

2 Nous avons selectionné 100 examens de crane de sujets non épileptiques *agés de 15 a 50 ans répondant a cette definition* Tous ont ete consideres comme normaux avec l optique de routine habituelle

3 Nous avons defini une methode de mensuration

4 50 % des examens ne se pretaient pas a des mensurations completes

5 Dans les 50 % restants nos recherches demontrent que l asymetrie crani enne est la regle Elle a un caractere extremement variable Chez un meme sujet, elle peut intéresser le diametre d une region d un coté et le diametre d une autre region de l autre cote Dans les conditions techniques que nous avons rappor tées les asymetries de diametre ne depassent pas 8 mm

Parfois l asymetrie n interesse qu un seul coté du crane, une moitie etant donc plus petite ou plus grosse que l autre Mais quelle que soit l importance de l asymétrie il ne s y associe jamais de modifications morphologiques con vergentes realisant un tableau analogue a celui decrit soit dans l hemi atrophie cerebrale soit dans certains hematomes sous duraux chroniques juveniles

Les termes d hypoplasie et de ballonnement ne se pretent donc pas a la de scription de l asymetrie normale

Les asymétries decrites par MacRae dans le tableau radiologique de l epilep sie non tumorale peuvent rentrer dans le groupe des asymetries normales

Dans l asymetrie normale il ne semble exister ni *predominance* de cote ni corrélation de siege avec les asymetries ventriculaires physiologiques

RÉSUMÉ

Par une méthode de mensuration qu il a précisée l auteur a étudié les asymétries craniennes Il a examiné les radiographies simples de 100 sujets agés de plus de 15 *ans non épileptiques* dont l encéphalographie fractionnée était normale La moitie seulement de ces cas se pretait à l appréciation objective d une asymétrie Ce travail montre que l *asymétrie est la règle* L auteur a recherché les signes quantitatifs et morphologiques qui permettent de la différencier de l asymetrie pathologique qui traduit une modification macroscopique du contenu cranien

SUMMARY

Cranial asymmetry was measured by a special method in conventional roentgenograms of 100 non-epileptics over 15 years of age with normal encephalograms Complete measure

ments were found to be possible only in about half the cases Asymmetry within certain limits appear to be the rule An attempt was made to find quantitative and morphologic changes bearing a relationship to the different degrees of asymmetry so that the significance of the latter in terms of the macroscopic structure of the cranial contents might be indicated

ZUSAMMENFASSUNG

Mit einer naher erlauterten Methode wurde an Übersichtsaufnahmen von 100 uber 15 Jahre alten, nichtepileptischen Patienten deren fraktionierte Enzephalographie normal war Messungen der Asymmetrie des Schadels vorgenommen Nur 50 % der Falle eigneten sich fur eine vollstandige Messung d h fur die objektive Erkennung einer Asymmetrie Die *Arbeit zeigt als Ergebnis dass die Asymmetrie die Regel ist* Der Autor versucht quantitative und morphologische Zeichen zu finden die sie von einer pathologischen Asymmetrie unterscheiden lassen Die Definition hierfur wird entsprechend der des normalen Schadels von den makroskopischen Veranderungen des Schadelinhalts abgeleitet

REFERENCES

Broca, P cité par Testut L et Latarjet A

Bull J W D Radiological diagnosis of chronic subdural hematoma Proc roy Soc Med 33 (1940), 203

— Diagnosis of chronic subdural hematoma in infant and adolescent Brit J Rad 22 (1949) 68

Childe, A E Localised thinning and enlargement of the cranium with special reference to the middle fossa Amer J Roentgenol 70 (1953) 1

Davidoff L M Masson C B and Dyke C Cerebral hemiatrophy with homolateral hypertrophy of the skull and sinus Surg Gynec Obstet 57 (1933) 588

Goalwin J cité par Ledoux Lebard G et Garcia Calderon, J

Hardman J Asymmetry of skull in relation to subdural collection of fluid Brit J Radiol 12 (1939) 445

Jackson H Asymmetry and growth of the skull Brit J Rad 29 (1956) 521

Jupe M H Reaction of bones of skull to intracranial lesions Brit J Radiol 11 (1938) 146

Lebon, G cité par Talairach J

Ledoux Lebard, G et Garcia Calderon J Technique de radiodiagnostic p 358 Masson Paris 1959

Lefèvre, J Guy E et Metzger J Evolution des signes radiographiques des atrophies cérébrales unilatérales Acta radiol 40 (1952) 314

Lindgren E Eine enzephalographische Formvariante des Seitenventrikels Acta radiol 22 (1941) 722

— Encephalography in cerebral atrophy Acta radiol 35 (1951) 277

Lombardi G Déformation crânienne par hématome chronique sous dural et par hydrome J Radiol Electrol 35 (1954) 854

MacRae, D L Focal epilepsy *correlation of the pathological and radiological findings* Radiology 50 (1948) 439

Olsson O Instrument for ensuring symmetric pictures in roentgen examinations of the head Acta radiol 31 (1949) 240

Porcher, P Précis de technique radiographique p 7 Gauthier Villars Paris 1948

Ross, J Cerebral hemiatrophy with compensatory homolateral hypertrophy of the skull and sinus and diminution of cranial volume Amer J Roentgenol 45 (1941) 332

RUGGIERO G Encéphalographie fractionnée p 170 Masson Paris 1957
— THIBAUT A HECAEN H et DELL M B Confrontation de données radiologiques neurologiques et électroencéphalographiques dans 26 cas d épilepsie non liés à un processus occupant de l espace intracranien R N radio-isotopes et E E G *dans l épilepsie* p 115 Masson Paris 1960
TALAIRACH J Chirurgie stéréotaxique du thalamus VIe Congres latino Américain de Neurochirurgie Montévideo (1955) 865
TESTUT L et LATARGET A Traité d anatomie humaine Tome I p 285 Doin Paris 1948
THIBAUT A Le tableau radiologique des collections liquidiennes encapsulées sous durales supratentorielles chroniques chez les jeunes Neurochirurgie 4 (1958) 180

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CALCIFICATION IN THE DISTAL RADIO-ULNAR JOINT

by

Johannes Thoms

Lang in his work on the distal radio ulnar joint describes a case of an osseous loose body in the recessus sacciformis Such a body may originate from a detachment of bony tissue from the radius or ulna, or from the cartilaginous surfaces of the bones or the articular disc Lang also mentions the possibility of 'joint mice' being formed in osteochrondritis dissecans, cases of which have been described by Thoms and Schoneich although the bodies were not situated in the recessus sacciformis Lang's patient had had a severe injury to the wrist and, in addition to arthritis of the carpal joints, there were marked osseous changes in the semilunar bone He considered that the semilunar bone had been fractured and that a detached fragment had made its way up into the radio ulnar joint through an existing or traumatic cleft in the disc As this lesion is uncommon a report of a further case would appear to be justified

A man, a potter aged 40 had for about two years been periodically troubled with pain in the left wrist, localized mostly to the dorsal aspect it had become worse and prevented him working No history of trauma On examination movements of the wrist caused pain but were not limited No tenderness swelling or crepitation

Roentgen examination of the left wrist revealed a dense rather irregular body about the size of a pea at the proximal margin of the radio ulnar articulation lying slightly dorsally No evidence of osteochrondritis dissecans arthritis or fracture Right wrist normal The patient was treated with radiotherapy (140 kV 10 mA 3 mm Al 100 r × 2 at 8 day intervals) following which the pain disappeared and he returned to work

Submitted for publication 12 December 1960



Pneumoarthrography of left distal radio-ulnar joint Calcification in recessus sacciformis.

The wrist is illustrated one month after the last treatment and following the injection of air The calcified body lies in the recessus sacciformis and the joint capsule and distal fibres of the interosseous membrane are not affected As the air was confined to the radio-ulnar articulation it is improbable that there was any communication between it and the recessus sacciformis

Discussion

This patient s work as a potter involved frequent supination pronation movements against resistance which are known to be a frequent cause of tendovaginitis crepitans There is probably some causal association with peritendinitis calcarea in such cases Tendovaginitis peritendinitis or bursitis accompanied by calcification in the tissue involved may in addition to the shoulder region arise around the hip knee and ankle (SANDSTROM MILLER) or more rarely in the fingers (JANSEN OLDFIELD) KIERULF reported seven cases of peritendinitis calcarea in the region of the wrist in which the calcifications disappeared completely or almost completely after roentgen treatment

The calcification in our case was presumably formed primarily in the wall of the recessus sacciformis and became detached from the synovial membrane The good effect of irradiation is in conformity with the suggested aetiology

SUMMARY

A case of calcification in the recessus sacciformis of the wrist shown by pneumoarthrography is described

ZUSAMMENFASSUNG

Ein Fall mit einer Verkalkung im Recessus sacciformis des Handgelenkes welche bei einer Pneumoarthrographie beobachtet worden war, wird beschrieben

RÉSUMÉ

Description d un cas de calcification du récessus sacciforme du poignet mise en évidence par pneumo arthrographie

REFERENCES

JANSEN K F Calcareous peritendinitis Acta radiol 24 (1943) 285

KIERULF E Peritendinitis calcarea i håndledsregionen (In Norwegian) Nord Med 45 (1951) 975

LANG F Das distale Radio Ulnargelenk Unfallheilkunde 36 (1942) 3

MILLER C F Occupational calcareous peritendinitis of the feet Amer J Roentgenol 61 (1949), 506

OLDFIELD M C Tennis thumb Tendinitis with calcification in flexor pollicis longus Lancet 1951 I, p 1151

SCHONEICH R Osteochondritis dissecans am Ulna Kopfchen Fortschr Rontgenstr 76 (1952) 268

THOMS, J Osteochondritis dissecans of the head of the ulna Acta radiol 34 (1950) 161

FROM THE ROENTGEN DEPARTMENT (DIRECTOR PROF J R BLICKMAN) AND THE DEPARTMENT OF PHARMACOLOGY (DIRECTOR PROF J H GAARENSTROOM) UNIVERSITY OF GRONINGEN, THE NETHERLANDS

ATROPINE COMBINED WITH CARBACHOL FOR PROMOTION OF GASTRIC PERISTALSIS

by

B G Dijken and D De Wied

The fact that gastric peristalsis is sometimes poor has led to attempts at its stimulation during the roentgenologic examination The first report on the use of drugs with which this can be effected was presented by Ritvo & Weiss in 1927 The great advocate of pharmaco roentgenology as a supplemental method of investigation however was Porcher (1946 1949 1952 1959)

Apart from pharmacologic stimuli to promote gastric motoricity electric psychogenic mechanical and thermal means have also been employed for this purpose By electric stimulation of the vagus nerve (by means of a catheter in the oesophagus) a very marked increase in motoricity can be effected (Stahnke & Severlein 1925) This method must be regarded as hazardous, however as it may result in disturbances in the cardiac rhythm Personal observations have shown that faradic stimulation of the associated skin segments as well as psychogenic and thermal stimuli produced no noteworthy effect We often observed a definite increase in motoricity following palpation of the gastric region after instructing the patient to take deep breaths, or after placing him in the prone position Before resorting to the use of drugs, it should be borne in mind that these should not produce any untoward or toxic symptoms and should be suitable for ambulatory patients The number of drugs or combined drugs mentioned in connection with this stimulation of peristalsis is relatively large although not all of them meet the necessary requirements

Submitted for publication 5 December 1960

RASMUSSEN (1950) was the first to use subcutaneous injections of atropine combined with prostigmine to increase peristaltic movements during the roentgenologic examination of the stomach ROLLANDI & SCARPONI (1951) and ROLLANDI (1953) reported on the intravenous administration of these drugs in combination

Personal observations

In view of reports in the literature on the use of atropine combined with prostigmine, we decided to study the effect of these drugs Since atropine is an antidote to prostigmine there is no pharmacologic objection to their combined use Intravenous administration might produce undesirable effects The effect was studied in 20 patients by injecting 0 5 mg atropine and 0 5 mg prostigmine subcutaneously from one syringe It was found that the desired motor effect remained absent and appeared to be inhibited by the preceding filling of the stomach and the examination of the patient in the upright position (See Table 1)

As prostigmine is the more active of the two drugs, another parasympathomimetic carbachol, which exerts its influence more directly, was selected This is a cholinester with a marked cholinergic action (KREITMAR 1932) Its most important sites of action in man are the musculature of the digestive tract, bladder and heart STEIN, MEIJER & STEIGMAN (1948) and HENNING, KINSELMEIJER & DEMLING (1952) registered the motor manifestations by introducing a balloon into the stomach It was found that carbachol caused a marked increase in motoricity even in patients who had undergone complete vagotomy It was also observed that carbachol, as compared with prostigmine, caused considerably more marked increase in peristalsis in normal test subjects

GOODMAN & GILLMAN (1955) reported that atropine should theoretically completely block the cholinergic innervation of the gastro intestinal tract They contended, however, that in practice this substance is known to counteract the effects of parasympathomimetics such as carbachol but to suppress only incompletely the effects of vagal impulses on the gastro intestinal tract

Examination of the motor effect in 65 patients showed that the subcutaneous injection of 0 5 mg atropine and 0 4 mg carbachol always caused a marked increase in peristalsis 8 to 15 minutes after their injection The filling of the stomach and the examination erect were found not to impair the effect The only side effect observed was the urge to urinate in 4 cases, the examination had therefore to be briefly interrupted in 2 cases Doses of 0 25 and 0 5 mg proved to be less satisfactory (Table 1)

It is advisable to reduce the dose of carbachol to 0 25 mg in cases of asthma as this substance may provoke an attack of dyspnoea (STARR 1937) In view of this fact, ten asthmatics who showed hypersensitivity to acetylcholine were submitted to a limited lung function test which revealed that a subcutaneous injection of 0 25 mg carbachol and 0 5 mg atropine was not contraindicated

Table 1

The effect of various drugs on motoricity in human subjects Patients with ectasia of the stomach from juxta pyloric stenosis not included

Subcutaneous injection	x 0.5 mg atrop sulf + 0.5 mg prostigmine before drinking the barium		xx 0.5 mg atrop sulf + 0.5 mg prostigmine after drinking the barium		xx 0.5 mg atrop sulf + 0.25 mg carbachol after drinking the barium		xxx 0.5 mg atrop sulf + 0.4 mg carbachol after drinking the barium		xxxx 0.5 mg atrop sulf + 0.5 mg carbachol after drinking the barium	
Number of observations	8		12		24		65		10	
	Prone	Standing	Prone	Standing	Prone	Standing	Prone	Standing	Prone	Standing
Increase in motoricity	8	8	11	8	24	21	65	65	10	10
No change in motoricity	0	0	1	4	0	3	0	0	0	0

x Insufficient peristalsis during one observation
xx » » » two different observations
xxx » » » » » » in 40 of 65 patients
xxxx » » » » » » » 6 » 10 »

The pharmacologic effect of the atropine carbachol combination It has been stated that a cholinergic effect on the gastric musculature occurs in man following the combined administration of a parasympathomimetic (carbachol) and a parasympatholytic drug (atropine) This observation is rather strange because atropine is the antidote par excellence against violent motor changes in the gastro-intestinal canal which may occur after carbachol treatment (Goodman & Gillman 1955) An attempt will be made to explain this apparent paradox by reports of investigations in rats and man and in vitro investigations on the human stomach

Investigations in rats The rat is the most suitable animal for experimental investigation of the gastro intestinal tract (Godlewski 1951) The size of the animals and their cost do not prohibit large scale investigations We used white female rats with an average bodyweight of 200 g 3 ml barium meal being introduced into the stomach by means of a Nelaton catheter No 10 the test animals then being placed in plastic tubes of 5 cm diameter Five of such tubes were fixed in a wooden rack Under these conditions it is possible by means of fluoroscopy and roentgenography to make continuous observations on the peristaltic phenomena and the emptying of the stomach As the test animals are sufficiently firmly fixed this arrangement renders anaesthesia unnecessary

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Personal observations

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Examination of the motor effect in 65 patients showed that the subcutaneous injection of 0.5 mg atropine and 0.4 mg carbachol always caused a marked increase in peristalsis 8 to 15 minutes after their injection. The filling of the stomach and the examination erect were found not to impair the effect. The only side effect observed was the urge to urinate in 4 cases, the examination had therefore to be briefly interrupted in 2 cases. Doses of 0.25 and 0.5 mg proved to be less satisfactory (Table 1).

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Table I

The effect of various drugs on motoricity in human subjects Patients with ectasia of the stomach from juxta pyloric stenosis not included

Subcutaneous injection	x 0 5 mg atrop sulf + 0 5 mg p ostigmine before drinking the barium		xx 0 5 mg atrop sulf + 0 5 mg prostigmine after drinking the barium		xx 0 5 mg atrop sulf + 0 25 mg carbachol after drinking the barium		xxx 0 5 mg atrop sulf + 0 4 mg carbachol after drinking the barium		xxxx 0 5 mg atrop sulf + 0 5 mg carbachol after drinking the barium	
Number of observations	8		12		24		65		10	
	Prone	Standing	Prone	Standing	Prone	Standing	Prone	Standing	Prone	Standing
Increase in motoricity	8	8	11	8	24	21	65	65	10	10
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Table 2

Roentgenologic observation in rats

Subcutaneous injection	0.4 ml 0.9 % saline	6.6 γ atrop sulf	6.6 γ carba chol	6.6 γ atrop sulf + 6.6 γ carba chol	2 × 6.6 γ atrop sulf and after 20 min 6.6 γ carbachol	50 γ atrop sulf	50 γ atrop sulf + 6.6 γ carba chol	50 γ atrop sulf and after 30 min 6.6 γ carbachol
Increase in motoricity	0	3[1]	10	10	9	0	10[4]	0
No change in motoricity	10	12	0	0	0	0	0	10
Decrease in motoricity	0	9[2]	0	0	0	10[3]	0	0

[1] moderate [2] 25 min after injection [3] 5 min after injection [4] moderate short lasting effect

We found that a subcutaneous injection of physiologic saline produced day to day variations in the motor manifestations of the stomach in the same animal We also noted a daily difference in the emptying rate These observations were confirmed during subsequent investigations in which the subcutaneous injection was always preceded by a 30 min period of observation No effect whatever was seen after a small dose of atropine The same quantity of carbachol, however, caused a marked *increase in the motor effect The motor intensity seen* after the combined administration of equal doses of both drugs did not differ *from that observed after the administration of carbachol alone* Nor was a difference noted when this quantity of atropine was given in advance Increased doses of atropine, however, caused a decrease in motoricity and after the administration of a large dose of atropine combined with a much smaller dose of carbachol there was, surprisingly, a moderate increase in peristalsis during a brief initial period, which was followed by atonia No increase in the motor effect occurred, however, when a large dose of atropine was given first and followed by carbachol after a certain interval (See Table 2)

These observations in rats warrant the conclusion that carbachol causes an *increase in motoricity and that this is not suppressed* by an identical quantity of atropine Atropine in a sufficiently high dosage inhibits the effect of carbachol, *but only after a certain interval*

Roentgenologic investigations of the human stomach In view of the above observations in rats, further investigations in human subjects were performed No decrease *in the motor effect in the stomach after the subcutaneous injection* of 0.5 mg atropine was seen until after 30 min In agreement with the observations made in rats, we *found no difference between the effect of a subcutaneous* injection of 0.5 mg atropine combined with 0.25 mg carbachol and that of 0.25 mg carbachol alone, during *the first 15 minutes However, when 0.5 mg* atropine was first given, followed after 20 min by 0.5 mg carbachol, the motor

Table 3

Study in 10 human subjects

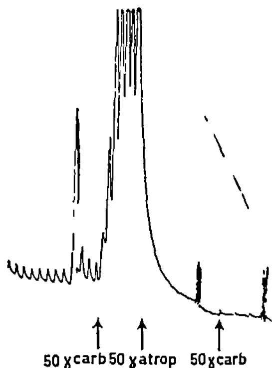
Subcutaneous injection	0 5 mg carbachol	0 5 mg atrop sulf + 0 5 mg carbachol
Fall in blood pressure	Syst 5 to 10 mm Hg Diast. 10 to 15 mm Hg	Syst 0 mm Hg Diast. 0 to 5 mm Hg
Sweat secretion	Marked effect	No effect
Heat sensations	Marked effect	No effect
Salivation	Moderate effect	No effect

effect of the latter drug proved to be completely blocked These observations show that also in man some time must elapse before atropine inhibits the motor effect of carbachol on the stomach

Blocking effect of atropine on the parasympathomimetic activity of carbachol It is a remarkable fact that after the subcutaneous injection of atropine carbachol an increase in gastric peristalsis occurs whereas none of the other phenomena associated with the administration of carbachol is seen In view of this fact we studied the general phenomena produced by this combination as compared with those produced by carbachol alone in the same test subject An examination of 10 subjects showed that the decrease in blood pressure hyperhidrosis, heat sensations and salivary activity observed after the administration of 0 5 mg carbachol do not occur (or to a much less marked degree) after this dose combined with 0 5 mg atropine The urge to micturate the urge to defaecate, and borborygmi were reported in the same frequency (See Table 3)

In vitro investigation of the human stomach This study was made with fresh surgical specimens obtained at partial gastrectomies for benign conditions of the stomach or the duodenum The resected specimen was washed off with 'perfusion fluid in which it was kept at a temperature of 4° C The investigation in the gastro intestinal tray took place 3 to 5 hours later The stomach was opened along the greater curvature A strip of the gastric wall 2 to 3 mm wide and 3 cm in length was cut off 3 to 4 cm in front of the pyloric region perpendicular to the longitudinal axis of the stomach The mucosa was dissected off after which the strip of muscle was suspended in the gastro-intestinal tray (Composition of fluid 16 g NaCl 0 4 g KCl 0 4 g $CaCl_2$ 0 3 g $MgCl_2$ 6 H_2O 2 g NaHCO 0 1 g NaH PO_4 2 H_2O 2 g glucose in 2 l distilled water temperature 37 C capacity of bath 5 ml)

A contraction was invariably seen after the addition of carbachol This however was immediately controlled and blocked by the addition of atropine as illustrated in the figure These observations therefore contradict the observations made in vivo



Effect of carbachol (50 γ per 5 ml) before and after the addition of atropine sulfate (50 γ per 5 ml) In vitro investigation of the human stomach Immediate spasmolytic effect of atropine during carbachol contraction

It has been shown in the above that when carbachol and atropine are simultaneously administered in equal doses, the latter drug does not immediately suppress gastric peristalsis, but immediately controls other signs produced by carbachol, namely decreased blood pressure, sweat secretion, heat sensations and salivation The parasympathomimetic effect of carbachol on the peripheral blood vessels and the sudoriferous and salivary glands is therefore more rapidly suppressed by atropine than are the motor phenomena of the visceral system This is in accordance with the in vivo effect produced by atropine alone The in vitro findings, which are not in agreement with this, may be explained by the presumption that under these conditions there is a difference in the susceptibility of the end organs to the inhibitory effect of atropine

Discussion

Morphine is the agent most frequently used to promote the motoricity of the human stomach Porcher et coll reported some 15 000 observations in which a subcutaneous injection of 10 mg was employed (Porcher, Stoszel & Bainquet 1959) Some 80 % of the cases showed increased motoricity for twenty minutes after the injection, this being followed by a phase of gastric atonia Similar observations were made by Sauvegrain (1946), Rasmussen (1949), *Albot & Corteville (1952)*, *Stoszel (1953)*, *Gimes (1955)*, and Pfeiffer (1956) We have refrained from using this drug because in these doses it can produce side effects such as collapse, nausea and vomiting (Porcher 1946, Porcher et coll 1949, Blondet et coll 1949, Rasmussen 1950, Albot & Corteville 1952) Taking into consideration that the motor effect remains absent in 20 % of cases, that the effect occurs only in the prone position and is not always observed when the stomach is filled with barium, it may be stated that this agent does not appear to be the one of choice for promoting gastric peristaltic movements

Albot, Renaux & Girard (1946) and Albot & Corteville (1952) administered 10 to 20 U insulin intravenously Porcher (1952) and Adler et coll (1955) *contended however that only a poor and not convincing increase*

in motoricity can thus be produced Since insulin at the dosage indicated produces disagreeable side effects and apparently does not always cause the desired result this agent must also be considered unsuitable

HENNING KINZELMEIJER & DEMLING (1952) administered the posterior pituitary extract Piton (Organon, Oss, Holland) and registered the increase in gastric peristalsis by the balloon method Gastroroentgenologic examinations by VELDE (1933) revealed first a decrease and subsequently an increase in motoricity, which suggests that this extract is not entirely satisfactory The hypersecretion and increased blood pressure and constriction of the coronary vessels caused by this agent must moreover contraindicate its use

An increase in tone and peristalsis is seen after the administration of acetylcholine in sufficiently large doses The dosage required, however is above the permissible limit, and the effect is not constant This is probably due to its rapid breakdown the reason why it is replaced for clinical purposes by more stable substances such as carbachol and urocholine

RITVO & WEISS (1927) & RITVO (1936) administered physostigmine orally (2 6 mg) or subcutaneously (1 3 mg) and found that the desired motor effect occurred in about 85 % of cases Since the maximal permissible dosage must be exceeded and the effect does not always occur, this substance does not appear an acceptable one for our purpose RASMUSSEN (1950) observed an increase in motoricity in 22 of 34 patients given a subcutaneous injection of 0 5 mg prostigmine (neostigmine) Corroborating reports were presented by VEACH, LAUER & JAMES (1938) who used an intravenous injection of 0 5 to 2 0 mg

There is no agreement as to the effect of atropine on the motoricity of the stomach Roentgenologic observations seem to indicate that in the case of atonia a moderate increase in gastric peristalsis occurs during the first 10 to 15 minutes followed by marked inhibition after about 30 minutes (VELDE 1933 SAUVEGRAIN 1946 DERIU 1949, PORCHER 1952) PORCHER pointed out that the motor effect is poor so that the more effective substance morphine should be preferred Our observations in 10 subjects showed that a subcutaneous injection of 0 5 mg atropine caused only a slight increase in motoricity in a few cases

With regard to the employment of a subcutaneous injection of atropine carbachol it can be stated that it invariably produces an increase in gastric peristalsis even after the stomach has been filled with barium and the patient is examined erect The absence of certain symptoms which occur after the administration of carbachol alone is fortunate and is in agreement with other investigations showing that the sensitivity of the postganglionic parasympathetic nerve fibres to atropine varies widely from organ to organ In dogs for example, the effect on the heart of electric stimulation of the vagus is completely controlled by the intravenous injection of 0 1 mg/kg bodyweight atropine, 0 5 to 1 5 mg kg is required to inhibit the salivation caused by electric stimulation of the chorda tympani Much larger doses are necessary to prevent contraction

of the urinary bladder as a result of stimulation of the sacral parasympathetic nerves (HENDERSON & ROEPKE 1937)

The fact that the urge to urinate occasionally necessitates a brief interruption of the examination is no contraindication to the use of this combination of drugs

SUMMARY

The subcutaneous injection of atropine combined with carbachol was found invariably to produce a marked increase in gastric peristalsis In vivo investigations in rats and human subjects showed that some time elapses before atropine inhibits the cholinergic effect of carbachol on the gastric musculature although it rapidly controls any side effects produced by the latter drug

ZUSAMMENFASSUNG

Die subkutane Injektion von Atrophin in Kombination mit Karbachol erzeugte standig deutlichen Anstieg der Magenperistaltik Untersuchungen an lebenden Ratten und Beobachtungen beim Menschen zeigten dass es eine gewisse Zeit dauert bevor das Atrophin den cholinergischen Effekt des Karbachols auf die Magenmuskulatur inhibiert, obwohl es alle Nebenwirkungen, welche durch die letztere Droge erzeugt werden schnell unter Kontrolle bekommt

RÉSUMÉ

Les auteurs ont constaté que l injection sous cutanée d atropine associée au carbachol augmente toujours de façon marquée le péristaltisme gastrique Les recherches in vivo sur des rats et des sujets humains on montre qu un certain temps s écoule avant que l atropine n inhibe l effet cholinergique du carbachol sur la musculature gastrique bien qu elle empeche rapidement les effets secondaires dus a ce produit

REFERENCES

ADLER D C JACOBSON G HEITMANN K A and WATSON D D Insulin induced hypermotility in the roentgen examination of the stomach and duodenum Radiology 65 (1955) 530

ALBOT G en CORTEVILLE M Pharmacoroentgenografie van maag en duodenum Belg T Geneesk 8 (1952) 673

— RENAUX J et GIRARD E Un nouvel agent pharmacoradiographique l insuline intraveineuse Arch Mal Appar dig 35 (1946) 118

BLONDET P BUFFARD P BRET P et ROCHE P La morphine par voie buccale en radiologie digestive J Radiol Electrol 46 (1949) 30

DERIU, G Prova farmaco dinamica coll atropina nella radiodiagnostica gastro duodenale Radiol med 35 (1949) 939

DIJKEN B G De waarde van peristaltiek bevorderende farmaca bij het rontgenologische *maagonderzoek* Thesis Groningen 1959

GIMES B Die Bedeutung der Pharmacoradiologie in der Differentialdiagnose des praepylorischen Ulcus Fortschr Rontgenstr 83 (1955) 771

GODLEWSKI M A la recherche d un animal réactif idéal pour les epreuves pharmaco dynamiques en radiologie digestive Arch Mal Appar dig 40 (1951) 234

— Action de la prostigmine sur le tube digestif radiologique de quelques animaux Arch Mal Appar dig 40 (1951), 796

GOODMAN L. S and GILMAN A The pharmacological basis of therapeutics The Macmillan Company New York 1955
HENDERSON V E and ROEPKE M H Drugs affecting parasympathetic nerves Physiol Rev 17 (1937) 373
HENNING N KINZELMEIER H und DEMLING L Fortlaufende Registrierung verschiedener Magenfunktionen beim Menschen unter dem Einfluss von sekretions und motilitatsfor dernden Substanzen Z ges exp Med 118 (1952) 177
KREITMAR, H Eine neue Klasse Cholinester Arch Path Pharmak. 164 (1932) 346
PFEIFFER, J Pharmacoradiografie des Magens Fortschr Rontgenstr 84 (1956) 421
PORCHER P L hyperkinésie gastrique provoquée Technique nouvelle de l exploration com plémentaire de l estomac et du bulbe duodénal J Radiol Electrol 27 (1946) 393
— Les modificateurs de comportement en radiodiagnostic digestif France med Gastro-entérol I (1952) 13
— STOSZEL H U und BAINQUET P Die klinische Untersuchung des Magens und des Zwolf fingerdarmes Thieme Stuttgart 1959
— BOURDON R BALDAGHIAN B et SAUVEGRAIN J Bilan de la morphine apres 6 000 examens Arch Mal Appar dig 38 (1949) 942
RASMUSSEN TH Pharmacoradiografi af ventriklen ved hjælp af morfin og ipecacuanha (Danish) Nord Med 41 (1949) 980
— Pharmacoradiografi af ventriklen (Danish) Nord Med 44 (1950) 1563
RIGLER M Drugs as an aid in roentgen examination of the gastro-intestinal tract. The use of mecholyl physostigmine and benzedrine in overcoming atonicity sluggishness of peristalsis and spasm Amer J Roentgenol 36 (1936) 868
— and WEISS S Physostigmine as an aid in gastro-intestinal roentgen ray diagnosis Amer J Roentgenol 18 (1927) 301
ROLLANDI A Ancora sull impiego della prostigmina ad atropina associate nello studio farma coradiologico dello stomaco e del duodeno Riv ital Radiol clin 3 (1953) 2
— e SCARPONI F L associazione prostigmina atropina nell esame radiologico dello stomaco e duodeno con particolare riguardo alla stenosi pilorica Minerva med (Torino) 2 (1951) 73
SAUVEGRAIN J Utilisation systematique de modificateurs de comportement en radiologie gastro-duodénale Thesis Paris 1946
STAHNKE E und SEIJERLEIN Elektrische Vagusreizung beim Menschen Munch med W schr 73 (1925) 334
STARR I Carbaminoylcholine (doryl or lentin) Its action on normal persons, in peripheral vascular disease and in certain other clinical conditions Amer J med Sci 193 (1937) 393
STEIN I F and MEYER K A The use of insulin in testing for completeness of vagotomy Surg Gynec Obstet 86 (1948) 473
— — and STEIGMAN F Changes in gastric motility and the effect on motility of following complete vagotomy Surg Gynec Obstet 87 (1948) 465
STOSZEL, H U Die klinische Bedeutung der Pharmacoradiografie ins besondere des Mor phins bei Erkrankungen des Magens und des Duodenums Schweiz med Wschr 83 (1953) 657
VEACH H O LAUER B R and JAMES A G Effects of prostigmine and atropine in the human stomach J Pharmacol 6? (1938) 422
VELDE G Die Magenschleimhaut bei Achylia Gastrica und perniciose Anaemie Ihr Verhalten auf vegetativen Reizen Ergebn med Strahlenforsch 6 (1933) 347

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GENERAL THEORY OF NARROW BEAM ROTATION TOMOGRAPHY

by

PEKKA SOILA

Narrow beam rotation tomography, panoramic tomography, or pantomography, has been developed to a practical and useful roentgenographic procedure by PAATERO (1949, 1954) This author has presented mathematical formulae of several aspects of pantomography (1954, 1956), and further mathematical data have been published by DUHAMEL (1955), HUDSON KUMPULA & DICKSON (1957), and VUORINEN (1959) These investigations have dealt with important aspects of pantomography, e g the positioning of the film, the thickness of the depicted layer, and the characteristics of an extremely narrow beam of radiation

Certain theoretical facts as well as the availability of equipment similar to pantomographs have necessitated a general investigation of the theory of this type of tomography It is well known that the transversal tomograph of VALLEBONA (1952) can be used for longitudinal tomography In the standard equipment the roentgen beam is directed horizontally, while the patient and the film are made to rotate vertically Such a method is in routine use wherever equipment based on this principle has been installed A full beam of radiation is employed and no investigations appear to have been published on

Submitted for publication 17 December 1960

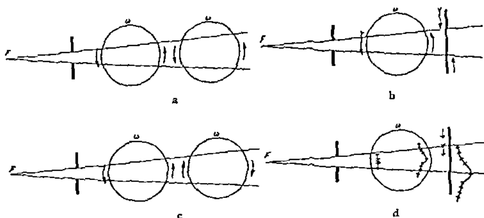


Fig 1 Various combinations in the application of narrow beam rotation tomography a) Vallebona type patient and film disk rotating in same direction beam is narrow but film curved b) and c) Variations of pantomography d) Two further developments of the technique.

the use of a narrow beam in combination with this adaptation Attempts to rotate the disks in opposite directions do not seem to have been recorded A general and relatively simple mathematical consideration of the theory of the various combinations of rotation tomography with special regard to the use of a narrow beam would therefore appear to be of interest and value

The possible combinations in the application of the technique are shown in Fig 1 In (a) the patient and film disks rotate in the same direction but the beam is limited and the film may be straight or curved The part nearest to the focus or the part farthest away will be depicted according to the position of the film The geometrical conditions are clearly more favourable in the latter case and in practice the corresponding variation has been most commonly used

The principle of pantomography with the disks rotating in opposite directions is exemplified in Fig 1c Obviously improved geometrical conditions are obtained by placing the film to the focus side of the film disk This was PAATERO s solution of the problem in his original communication (1949) Other uses of this method may however be of importance An enlarged image may for example be obtained by placing the film on the far side of the film disk and calculating the layer to be depicted from the focus side of the object The conditions obtained in Fig 1a obviously represent a middle road solution between the two extremes provided by pantomography Certain problems connected with optimal blurring may be approached by a consideration of the positioning of the patient in relation to the rotation axes

Another variation of pantomography is shown in Fig 1b, originally suggested by PAATERO (1955) especially for stereo pantomography, and later put into practical use by HUDSON et coll as well as by the present author This method is

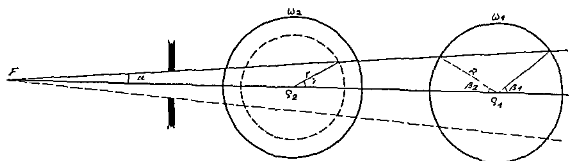


Fig 2 Combination of the variations presented in fig 1 (a) and (c)

useful as no curved films are needed but it also makes possible the use of the focus side of the patient disk, as suggested above These possibilities are illus trated in the drawing by similar arrows The small error caused by flattening the film will be dealt with below

Two further developments of the technique are presented in Fig 1d Panto mography has so far been used practically exclusively in examinations of the jaws The longitudinal variation of the technique of VALLEBONA has been performed with a full beam of roentgen rays, a flat film traversing the beam during a continuous change of angle between it and the central ray PAATERO (1956) also published an investigation of pantomography of flat layers, in which a *rotating film disk and a varying central ray film angle were employed* The use of the narrow beam rotating methods in other fields of medical roentgeno graphy should be planned with due consideration to the possibility of depicting other than cylindrical or similar simple curved layers In variation (b) as well as in the modification (d) the central ray and the film are perpendicular to each other during the whole exposure This arrangement also makes possible the de piction of a great number of varying layers In (d) the focus side layer of the object in effect reproduces a flat layer on a flat film, with preservation of the perpendicular central ray film angle The film side layer of the object illustrates the possibility of depicting an arbitrary layer in a film moving at a changing and corresponding speed Only layers with a curve approaching the direction of the central ray present difficulties in this modification of the technique while a great number of mathematical or otherwise prearranged layers may obviously be depicted

The variations in Fig 1, a and c, are combined in Fig 2 from which the following equations for the angles β and γ may be obtained

$$\beta = \overline{\arcsin}\left(\frac{\varrho_1}{R}\sin a\right) \pm a$$

$$\gamma = \overline{\arcsin}\left(\frac{\varrho}{r}\sin a\right) \pm a$$

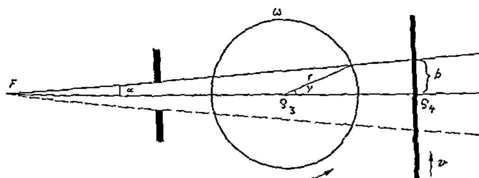


Fig 3 Variation of the solution presented in fig 1b based upon the use of a flat cassette

The + and — signs obviously provide four combinations of rotational movements in all which correspond to the four alternatives presented in Fig 1, a and c Provided the object disk and the film disk rotate at angular velocities ω_2 and ω_1 the times t_2 and t_1 for a given point of the object and for a given point in the film to traverse through the roentgen beam are as follows

$$t_1 = \frac{\beta(r)}{\omega_1} \quad \text{function of } r \quad t_2 = \frac{\gamma}{\omega_2}$$

The time difference t_1—t_2 between the traversing time of an object point and a film point is as follows

$$\left| t_1 - t_2 \right| = \left| \frac{\beta}{\omega_1} - \frac{\gamma}{\omega_2} \right|$$

This time difference is caused by divergence of the roentgen beam, the blurring and the dimensions of the image layer may be calculated with the help of the time difference as follows

$$\Delta s = (t_1 - t_2)\, R\omega_1 \quad \Delta s \leqq d$$

In the equations the letter d indicates the resolution of the film meaning the minimum distance between two points in the film for these to be resolved

The distance R that is the position of the film for depicting a desired layer of the object may be obtained as follows

$$\frac{\sin\beta}{\sin\gamma} = \frac{\frac{\varrho_1}{R} \pm \cos\beta}{\frac{\varrho_2}{r} + \cos\gamma} \quad \text{or}$$

$$R = \frac{\varrho_1}{\mp\cos\beta + \frac{\sin\beta}{\sin\gamma}\left(\frac{\varrho_2}{r} + \cos\gamma\right)}$$

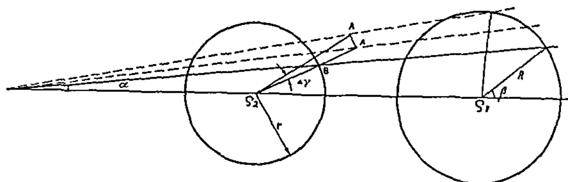


Fig 4 Geometrical relations

A variation of the alternative in Fig 1b, based upon the use of a flat cassette, is presented in Fig 3 Its advantage, apart from the convenience of its use, is the simplification in the positioning of the object in relation to the focus and the film It is possible to choose the position of the object to suit the requirements of the examination, while the relevant calculations and the handling of the film become relatively simple

The following equation may be derived from Fig 3

$$b = \varrho_3 \, tg \, \alpha = \frac{\varrho_4 \sin \gamma}{\varrho_3 - r \sin \gamma} \, r$$

$$t = \frac{b}{v} \quad \text{or generally} \quad t = \frac{b}{\bar{v}}$$

$$\bar{v} \text{ is the mean velocity} \quad \bar{v} = \frac{1}{t_0} \int^{t} v \, dt$$

The image layer $\Delta r = r' - r''$ may be calculated with the help of the time difference $t_1 - t_2$ from the condition $\Delta b \leq d$, where

$$\Delta b = b' - b'' = \frac{\varrho_4 \sin \gamma}{\varrho_3 - r' \cos \gamma} \, r' - \frac{\varrho_4 \sin \gamma}{\varrho_3 - r'' \cos \gamma} \, r''$$

As stated above the layer of the object to be depicted as well as the corresponding speed of the film may follow the course of several geometrical surfaces or other prearranged paths

The depicting capacity of the method is dependent upon the directions of the central ray and the layers to be depicted being parallel or nearly parallel to each other The following approach may be considered for this case (for the geometrical relations, see Fig 4)

The points A and A', are separated by the radial difference Δr This difference has an upper limit at which these two points will be clearly represented in the

film This condition may be expressed in a mathematical formula with the help of differential calculus

$$|\Delta r| \geqq \frac{\frac{\varrho}{r}\cos\beta_1 + \cos\gamma\cos\beta_1 + \sin\gamma\sin\beta_1}{\sin\beta_1} \cdot \frac{r^2}{\varrho_2}\frac{d}{R}$$

where d indicates the resolution in the film

The points A' and B must be a minimum distance apart in order to be clearly represented This gives the condition

$$\frac{\cos(\gamma-\alpha)}{\cos(\gamma+\alpha)} \cdot \frac{\frac{\varrho_1}{R} + \cos\beta_1}{\frac{\varrho_2}{r} + \cos\gamma} \, r\Delta\gamma \geqq d$$

Combining these two conditions we obtain the minimum value for the angle O between the line AB and the radius $\bar{r}$

$$O \geqq \text{arc tg}\left\{\frac{\sin\gamma}{\frac{\varrho_2}{r}\cos\beta_1 + \cos(\gamma+\beta_1)} \cdot \frac{\cos(\gamma+\alpha)}{\cos(\gamma-\alpha)}\frac{\varrho_2 R}{r^2}\right\}$$

The equations for β_2 may be written with the substitution

$$\beta_1 = \pi - \beta_2$$

It is evident that the angle of divergence plays an important role in every practical application of rotation tomography Experiments are now in progress to verify the validity of the theoretical considerations and to investigate the effect of the angle of divergence in the different combinations

This investigation was carried out during the author s tenure of a James Picker Foundation Research Fellowship at the Central Hospital Turku University Finland and Karolinska Sjukhuset Stockholm Sweden

SUMMARY

A theoretical generalization of the various types of rotation tomography in practical use is presented The developed formulae cover certain problems of optimal conditions for reproduction of the part of the object required

ZUSAMMENFASSUNG

Eine theoretische Verallgemeinerung verschiedener praktisch angewendeter Methoden der Rotationstomographie *wird vorgelegt Die entwickelten Formeln* ermöglichen die Lösung einiger Probleme der Rotationstomographie welche die optimalen Abbildungsverhältnisse behandeln

RÉSUMÉ

L'auteur présente une théorie générale des divers types de tomographie rotatoire utilisés en pratique Les formules qu il propose permettent de résoudre certains problèmes concernant les conditions optimales pour reproduire la partie de l objet a examiner

REFERENCES

DUHAMEL, J Les procédés de radiographie en coupe non rigoreux Sci Indust phot 25 (1954) 129

— Une forme nouvelle de phototomographie La photopantomographie de Y V Paatero Sci Indust phot 25 (1954), 353

HUDSON D C, KUMPULA, J W and DICKSON, G The panoramic X ray dental machine U S Armed Forces Med J 8 (1957), 46

PAATERO Y V A *new tomographical method for radiographing curved outer surfaces* Acta radiol 32 (1949) 177

— Pantomography in theory and use Acta radiol 41 (1954) 321

— Theoretico experimental study on the origin of the stereoscopic effect in pantomography Suom Hammaslaak Toim 50 (1954) 193

— On the pantomography of straight layers Suom Hammaslaak Toim 52 (1956) 84

— The principles of the construction and function of the stereopantomograph Acta radiol 43 (1955), 113

VALLEBONA A Trattato di stratigrafia Vallardi Ed Milano 1952

VUORINEN P *The roentgenographic slit methods Acta radiol* (1959) *Suppl No* 177

INSTITUT UND POLIKLINIK FUR PHYSIKALISCHE THERAPIE UND RONTGENOLOGIE (DIREKTOR PROF DR H VON BRAUNBEHRENS) DER UNIVERSITAT MUNCHEN, DEUTSCHLAND

RADIATION EXPOSURE IN BODY SECTION RADIOGRAPHY

by

F E STIEVE

A large number of recent investigations which were discussed at length during the last International Congress of Radiology have shown that at the present time diagnostic roentgen examinations still make by far the greatest contribution to the total amount of artificially produced ionizing radiation received by the population Results presented so far particularly those in the reports of the National Academy of Sciences the National Research Council the British Medical Research Council and the International Commission for Radiological Protection (ICRP), as well as in the works of ARDRAN HAMMER JACOBSON OSBORNE & SMITH LARSSON MOHR and my earlier colleague SEELENTAG predominantly contain general statistical data and measurements relating to the radiation exposure of man in routine roentgen examinations There has been no detailed study however of radiations exposure during specialized forms of examination such as tomography For this reason Sub-Committee IV (Body section Equipment) of the International Commission on Radiological Units and Measurements (ICRU) was given the task of carrying out such a study and reporting the findings Within these terms of reference the following points were investigated in the various systems used for producing longitudinal body section roentgenograms

Based on a paper read at the 4th International Course on Stratigraphy in Genova Submitted for publication 15 November 1960

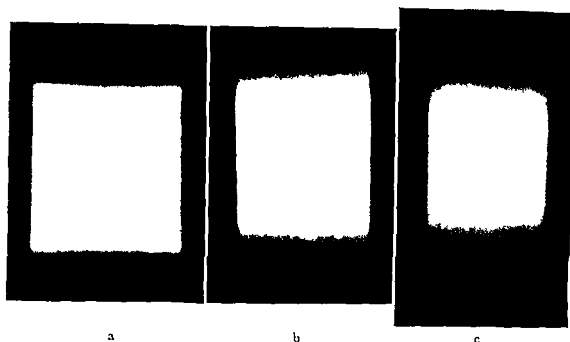


Fig 1 Field size and dose distribution at the surface near the roentgen tube for different section depths (3 9 5 and 16 cm) in planigraphy with linear movement of tube and film (Universal Planigraph FFD 140 cm pendulum angle 38° phantom thickness 20 cm 80 kV 2 mm Al)

1 The surface dose received by the body in the irradiated area,

2 The dose distribution in the body, in the area of the cone of useful radiation and its immediate surroundings,

3 The radiation received by the gonads during tomography

Before dealing with these results in detail we shall make a few comments on the subject of technique

Following the proposition of FRANKE, and since purely diagnostic problems were entailed, all dose values were quoted with reference to the dose received at the film (or, more accurately, at the front screen) and this was the same in all cases As experiments by HERZ, SPIEGLER, STIEVE, WIDENMANN and others have shown, in the voltage range 50 to 150 kV, used in diagnostic work for constant film density, with intensifying screens on a calcium tungstate basis of an average intensification factor (high definition and universal screens), a constant dose is required at the front screen The same applies to sectional radiography (WIDENMANN) During our measurements, the reference dose was 1 mr Our experience and measurements show that nowadays with the use of fast films and an efficient developer, the average dose can in practice be much lower

Tests made by MORGAN SCHOBER and myself in the course of density calibrations of automatic exposure devices indicate that the average density of a well exposed film lies around 0 7 and 0 8 To produce this density a dose of 0 5 to 0 6 mr is necessary

All dose measurements were made with a kondiometer from the physics and technology laboratories at Freiburg operating on the Sievert condensation chamber principle Results of measurements with this kondiometer are reproducible with an accuracy of approximately ± 3 %

A number of 10 mm spherical chambers were used for dose measurements on the surface and within the phantom (in spite of the often irritating lack of sensitivity) since it was required to assess the dose at a large number of positions at the same time Measurements of the dose to the gonads in cadavers and living subjects were carried out with 33 mm cylindrical chambers as was also the dose at the film In addition to high sensitivity these offer the advantage of being practically independent of the wavelength on the exit side over the voltage range employed

I Surface dose measurements

Many studies have been made of the surface dose in the irradiated field during routine roentgen examinations among which those of WACHSMANN and SORRENTINO should be mentioned They were principally concerned with the incident dose as a function of voltage, wave form pre filtration and focus/skin distance (FSD) and results were presented in the form of alignment charts The dose distribution in the field of radiation is almost uniform in the case of narrow beams such as are used in tomography A certain dose reduction is observed towards the anode side owing to the higher selfabsorption of the anode in this direction (FUCHS SCHAAL) Beyond the margins of the field the dose decreases very rapidly

During section radiography of a recumbent patient with tube and film moving the size of the irradiated field and the dose distribution differ from those found with a stationary tube The linear blurring in a system in which tube and film move along parallel lines is shown in Fig 1 the layer depth being adjusted by variation of the height of the centre of rotation while the focus/film and focus/skin distances remain constant (This system is used mainly in the Universal Planigraph and similar planigraphic equipments) The average angle of sweep which naturally varies with the depth of the layer is around 38 The dose distribution was determined from films obtained at the surface of a water phantom having the shape of a human trunk of 20 cm thickness at section depths of 3 9 5 and 16 cm and with a field of 20 × 20 cm at the film It may be seen from these three images that the area of the irradiated field becomes greater (in the direction of tube movement only) as the section plane shifts away from the tube side of the patient Since on geometrical grounds the positioning of the patient for tomography is normally such that areas of

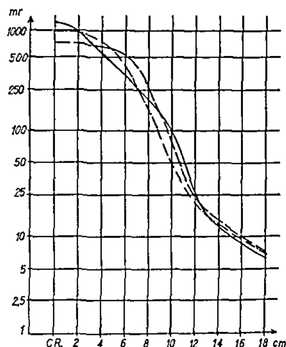


Fig 2 Dose in mr at centre line of surface at 3 cm (——) 9 5 cm (— —) and 16 cm (— —) layer depths

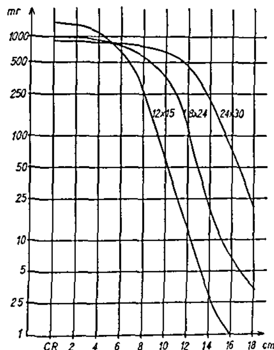


Fig 3 Dose in mr at centre line of surface with different field sizes Layer depth 9 5 cm

diagnostic interest are near to the film, we have generally, when using this technique, to reckon with a more widespread skin dose than in stationary field exposures Furthermore, there is usually a dose maximum in the centre of the field during sectional exposures

A corresponding picture of the surface dose distribution at the same section depths are given in milliroentgens in Fig 2 in which the region covered by the primary beam is indicated as well When the body section is close to the tube side, the surface dose conditions of the irradiated field are the same as is customary in survey radiography The dose fall off outside of the primary beam is extremely steep, the dose being reduced to about one hundredth of the incident dose at a distance of 6 cm or so from the margins of the field The further distant the section plane is from the surface of the body, the more marked is the dose maximum in the centre of the field, with a shallow peripheral fall off Despite a varying fall off of the dose in areas bordering the irradiated field, equal values are to be found at about 14 cm distance from the centre, i e about 6 cm from the margins of the field with the tube in median position

In systems where tube and film move through an arc, and where the distances from focus to rotational centre and from rotational centre to film remain the same (e g polytome and tomograph), the distance from the rotational centre

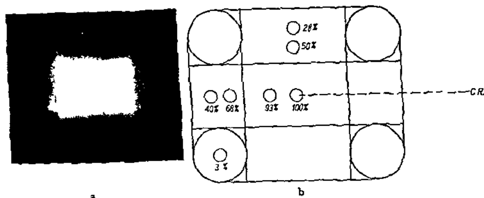


Fig 4 Field size (a) and percentage dose distribution (b) on the body surface at circular movement of roentgen tube and film (Polytome FFD 140 cm layer depth 9 5 cm pendulum angle 44 field size (film) 18 × 24 cm phantom diameter 20 cm)

to the film must be made greater than in the above mentioned system, since the subject film distance must be variable This means that at the same layer depths the subject is nearer to the tube (and the incident dose consequently higher) but although the size of the field of radiation is the same at the film the irradiated area of the skin of the subject is smaller While in the centre of the field approximately similar relationships are found with both systems for the incident dose at the various section depths the variations in surface dose obtained with the use of the latter system at different section depths will be maintained for areas outside the margins of the field Moreover the lack of homogeneity of the dose distribution over the whole field, with a maximum in the middle as compared to the borders of the field, is not so marked for sections nearer to the film This might be due to the smaller variations in FSD when the tube moves through an arc

It is self evident that in both systems the dose distribution at the margins of the field are also influenced by the size of the angle of sweep The greater the angle of sweep the larger is the area of skin exposed to direct surface radiation the smaller is the dose maximum in the centre and the steeper the dose fall off at the margins of the field

It should also be noted that with the same field size the mAs value is about 30 % higher in section radiography than in survey radiography under identical conditions this is not however accompanied by a corresponding increase in the average surface dose This fact remains to be further explained The reason can probably be sought in the greater distance from the tube to the point of incidence of the rays during part of the movement

The surface dose distribution naturally also varies with the field size This is shown in Fig 3 for fields 12 × 15 cm, 18 × 24 cm and 24 × 30 cm at a

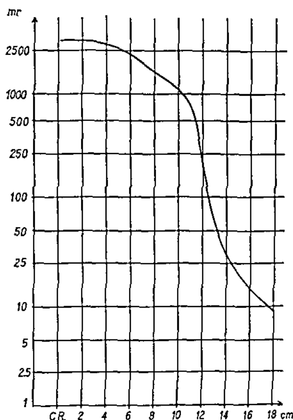


Fig 5 Dose at centre line of surface Other details as in fig 4

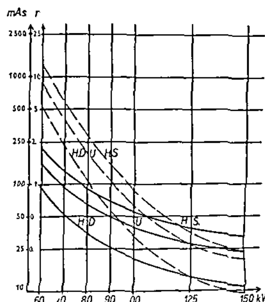


Fig 6 Incident dose and mAs values as functions of the kilovoltage for 3 types of intensifying screens related to a constant film blackening D = 1 0 (Linear blurring Universal Planigraph FFD 140 cm pendulum angle 38 grid of the ratio 12 5 1 Kodak Regulix film total filtration 2 mm Al)

H S — High speed intensifying screen U — Universal screen H D — High definition screen

— — — — — — Incident dose
———————— mAs values

layer depth of 9 5 cm and with the same angle of sweep It may also be seen that with the same dose at the film the incident dose decreases with increasing field size as a result of the increase in radiation scatter at the film, this phenomenon was described by WILSLEY for stationary field conditions as long ago as in 1924 However, the increase in surface dose with decreasing field has its limits in section radiography If the irradiated field x becomes smaller than double the distance d of the plane of section from the surface, times the tangent of one half the sweep angle α (critical case when $x = 2d \ \mathrm{tg}\ \frac{\alpha}{2}$), then no surface area is constantly in the beam of radiation during the period of exposure Although it occurs but seldom, such a condition is for instance found in section radiography of the ear, using a small field The size of the field appears, on the other hand, as the curves run practically parallel to have little effect on the dose fall off in the marginal areas Things become far more complicated when the blurring occurs in several dimensions As an example, the dose distribution for an exposure in section radiography using a polytome with a field size 18 × 24 cm at the film, a sweep angle of 44° and circular blurring is shown in

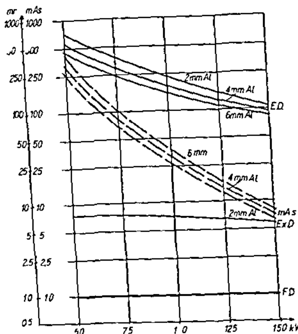


Fig 7 Incident dose and mAs-values as functions of the kilovoltage at different filtrations Other data as in fig 6

E D (—) Incident dose
— — — — — mAs values
Ex D (—) Exit dose behind phantom
F D — Film dose

Fig 4a The layer depth is again 9 5 cm Here too, we find a dose maximum in the centre in all cases except the smallest field (in the sense given in the definition above) The peripheral dose fall off is on the other hand rather irregular The percentage surface dose distribution was measured by means of condenser chambers after the dose maxima and minima had been determined (Fig 4b) Reductions of up to 30 % appear in the lateral sections the total field is larger and the dose curve in the longitudinal section (Fig 5) is not as regular as with linear blurring The peripheral fall off can be seen at about 10 cm from the centre of the field and this is also apparent in the films

Up to now we have only been comparing the doses at one voltage We know from numerous experiments with high voltage techniques (e g by Frik Gajewski Mattson and Wachsmann) that the incident dose is a function of the kilovoltage used and varies inversely The relations between incident dose, mAs-value and voltage in sectional exposures using systems with parallel movements of tube and film are illustrated in Fig 6 The FFD is 140 cm and

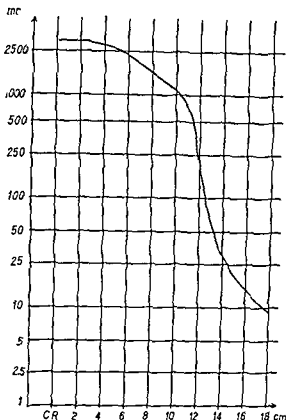


Fig 5 Dose at centre line of *surface Other* details as in fig 4

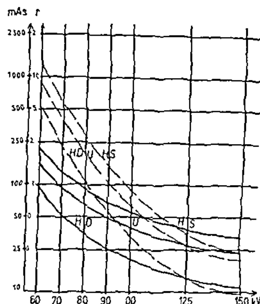


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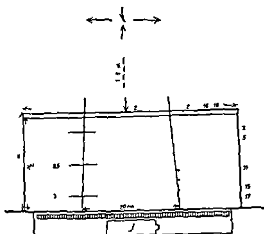


Fig 9 Measuring scheme to determine the dose in a phantom (20 cm thick water phantom film field size 20 × 20 cm FFD 140 cm reference dose 1 mr at the film)

J — Ionization chamber

of single exposures using a universal screen and the same kilovoltage so that a comparison was drawn of the dose requirement behind the subject and diaphragm in front of the first screen The results showed that there is no very great difference between the dose needed for a simultaneous series and for the same number of single section exposures Intensifying screen sets intended for use at higher voltages do bring about a somewhat larger reduction of dose due to the greater penetrating power of the harder rays The fact that screen sets for simultaneous series frequently call for the use of higher voltages and thus involve a reduction of the incident dose compared to single exposures (generally made at a lower voltage) cannot be put forward as an advantage of the multisection technique it is rather one of the wellknown advantages of using high kilovoltages It can of course equally well be used for single exposures in section radiography

Summing up we may say that the surface dose received during section radiography is of the same order as that received in survey radiography, although the dose is distributed over a larger irradiated field Dose requirements are governed by the same laws as apply to general radiography

II Dose distribution within the body

The study of the dose distribution within the body was intended to clarify the question of the location of the dose maximum and in particular to discover whether a dose concentration must be expected within the body, as is the case in moving field irradiation A comparison of the radiation scatter outside the limits of the beam with that occurring under similar conditions during exposures for a general radiographic survey was also to be made From a purely theoretical viewpoint it would not appear relevant to draw parallels as therapy

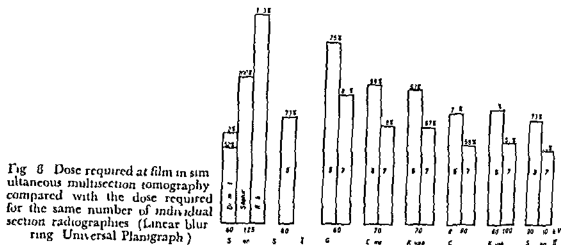


Fig 8 Dose required at film in simultaneous multisection tomography compared with the dose required for the same number of individual section radiographies (Linear blurring Universal Planigraph)

the sweep angle 38° In this case we did not, as elsewhere, take as a point of reference a constant dose of 1 mr but used a constant film density obtained with screens giving normal and high intensification as well as high definition screens While the curves for mAs and dose run almost parallel for the first and last mentioned types of screen, those obtained with the high intensifying screen fall off steeply with higher voltage Since universal screens call for the same dose to produce a given film density, irrespective of the voltage, this demonstrates the voltage dependence of the intensification factor already recognized in various other studies

An increase in prefiltration, and consequent alteration of the quality of radiation, which was once a subject of much discussion, will if used with the already comparatively strong overall filtration common nowadays (approx 2 mm Al) bring about a reduction by 20 % of the incident dose for a supplementary filter of 2 mm Al At the same time more exposure will be needed because of the reduction of the radiation emitted Therefore, and in line with STANFORD's recommendations for survey radiography, a total filtration of 3 mm Al should not be exceeded in section radiography with voltages below 100 kV

We shall finally mention one point in this connection which has been widely discussed of late that of keeping the dose low by means of the simultaneous multisection technique While this does offer a number of incontestable technical advantages, experiments carried out by my colleague, Miss WIDENMANN, contradict the widely held contention that it achieves a substantial reduction of the dose (BACKLUND, GAJEWSKI, LIESS, and others) Fig 8 shows the dose requirement of a number of commercially available multisection intensifying screen sets, and serves to bear out the findings of WIDENMANN on this point The reference value in these experiments was the dose for an equivalent number

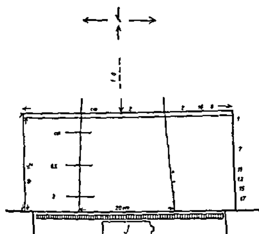


Fig 9 Measuring scheme to determine the dose in a phantom (20 cm thick water phantom film field size 20 × 20 cm FFD 140 cm reference dose 1 mr at the film)

J — Ionization chamber

of single exposures using a universal screen and the same kilovoltage so that a comparison was drawn of the dose requirement behind the subject and diaphragm in front of the first screen The results showed that there is no very great difference between the dose needed for a simultaneous series and for the same number of single section exposures Intensifying screen sets intended for use at higher voltages do bring about a somewhat larger reduction of dose due to the greater penetrating power of the harder rays The fact that screen sets for simultaneous series frequently call for the use of higher voltages and thus involve a reduction of the incident dose compared to single exposures (generally made at a lower voltage) cannot be put forward as an advantage of the multisection technique it is rather one of the wellknown advantages of using high kilovoltages It can of course equally well be used for single exposures in section radiography

Summing up we may say that the surface dose received during section radiography is of the same order as that received in survey radiography although the dose is distributed over a larger irradiated field Dose requirements are governed by the same laws as apply to general radiography

II. Dose distribution within the body

The study of the dose distribution within the body was intended to clarify the question of the location of the dose maximum and in particular to discover whether a dose concentration must be expected within the body as is the case in moving field irradiation A comparison of the radiation scatter outside the limits of the beam with that occurring under similar conditions during exposures for a general radiographic survey was also to be made From a purely theoretical viewpoint it would not appear relevant to draw parallels as therapy

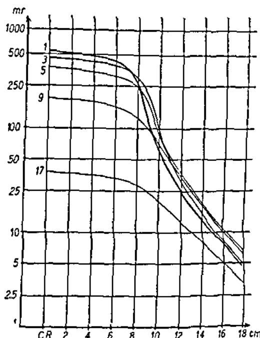


Fig. 10. Dose distribution in the phantom (20 cm of water) at different distances from the surface referred to a constant dose of 1 mr on the film grid of the ratio 12.5:1. 80 kV. Survey radiography.

The numbers at the dose distribution curves indicate the distance of the measuring points from the surface.

techniques involve considerably harder radiation, smaller fields and larger angles of sweep. If a correspondingly small angle were to be used in moving field therapy, a dose maximum at the skin could also be expected. A comparison was made with stationary fields of the same size, also using a grid and again taking a constant dose at the film as a reference. Measurements were made in a water phantom 20 cm thick with the Universal Planigraph, using a field of 20 × 20 cm at the film, the average sweep angle being 38°. As will be seen from Fig. 9, measurements were made at 1 cm below the water level and at 2 cm intervals down to 17 cm. Ten chambers were used in a horizontal direction, starting in the beam centre and spaced 2 cm apart; this meant that with the tube stationary, half of them were within the primary beam, and half outside.

The dose pattern with a stationary field at 80 kV is shown in Fig. 10. The dose distribution inside the cone of radiation matches the curves plotted by WACHSMANN, and is familiar from works by e.g. CEN and FRIK, JOHNS, KLOTZ, and SEELENTAG et coll.

The latter authors studied these relationships with 35 cm FSD, which gives a much sharper fall off in intensity within the phantom. They furthermore related the incident dose to a constant exit dose, while in the present measurements account was taken also of the diaphragm factor, which alters with the voltage. This means that the exit dose, related to a constant dose behind the grid (grid ratio = 12 : 1), falls by 60 % when the voltage is raised from 50 to 150 kV. Because of the alteration of the relation incident/exit dose, and as a result of the different beam path caused by the greater distance, the pattern of the dose

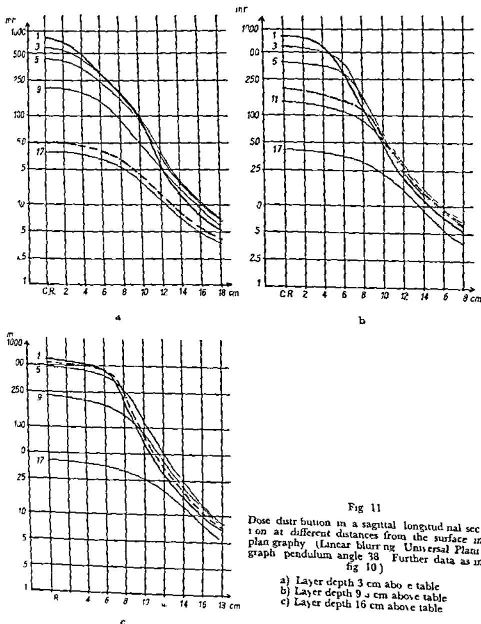


Fig 11

Dose distr bution in a sagittal longitud nal sec t on at different distances from the surface in plan graphy (Linear blurr ng Universal Plani graph pendulum angle 38 Further data as in fig 10)

a) Layer depth 3 cm abo e table
b) Layer depth 9 .5 cm above table
c) Layer depth 16 cm above table

outside the area of direct radiation is also rather different In principle how ever the curves obtained are similar to those recently presented bv HAYBITTLE and MARTIN and EVANS

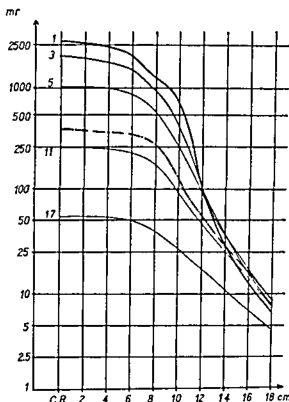


Fig 12 Dose distribution in a sagittal longitudinal section at different distances from the surface with multi dimensional blurring (Polytome circular blurring pendulum angle 44 FFD 140 cm extrafine grid field size 18 × 24 cm layer depth 9 5 cm Other data same as in fig 10)

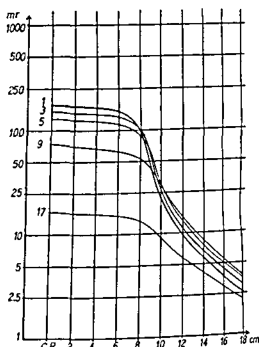


Fig 13 Dose distribution in a sagittal longitudinal section at different distances from the surface with a stationary field (Radiographic kilovoltage 130 kV Other data same as in fig 10)

A comparison of the dose distribution within a phantom, using the stationary field technique, and the section technique with a Universal Planigraph with tube and film moving parallel, at section depths of 3, 9 5 and 16 cm (Fig 11), gave the following results

The increased dose in the centre of the field, already observed at the surface, is also found in similar fashion in the upper parts of the phantom down to approximately its middle The greater the section depth, the greater is the dose increase at the centre of the field Connected with this are (1) a reduction of the plateau of the incident dose curve, as seen with stationary fields to produce a peak at the 3 cm level, and (2) the different dose fall off in surrounding areas, the curve being flatter compared to the sharper fall off found with a stationary field With linear blurring there is also for the various sections a dose reduction towards the margins of the field, *increasing with the depth of the section*, which can no doubt be mainly attributed to the difference in scattering at the centre and at the margins of the field (a phenomenon demonstrated by ZIELER

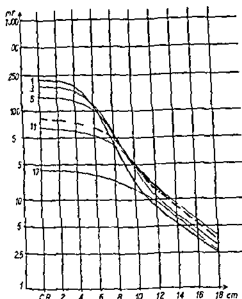


Fig 14 Dose distribution in a sagittal longitudinal section at different distances from the surface linear blurring (Radiographic kilovoltage 130 kV layer depth 9 5 cm other data same as in fig 11)

for a stationary field) The dose pattern for deeper parts of the phantom at small section depths approximately from middle of phantom downwards is similar to that of a stationary field this may be due to the patterns of the primary beams being similar At greater section depths, for which the area of primary radiation in lower parts of the phantom increases, the doses are higher making *the overall dose curve more shallow* The radiation outside the direct ray region at the 3 cm and 9 5 cm sections is the same as for a stationary field both in the upper and deeper parts The curves of the three measuring series correspond at a distance of about 12 cm The differences between the stationary field with its sharp dose fall off and the sectional field with a more gentle dose curve, were most apparent in the upper parts of the phantom where they out cancelled each other The conditions differ completely when the section plane is near the tube side of the phantom As a result of the shift of the beam of useful rays and the consequent spread of the area of direct radiation to both sides in the direction of the tube sweep the dose is then increased right out to the furthermost lateral point measured 18 cm from the centre of the field

The opposite is found as regards radiation scatter outside the field in the case of systems such as the polytome in these systems it is seen to be rather greater in section areas near the film than in those further away from it This is approximately similar to the dose at the surface In both systems then the fundamental difference between stationary and moving fields is a loss of uniformity of the dose over the irradiated field at the surface and nearby areas, together

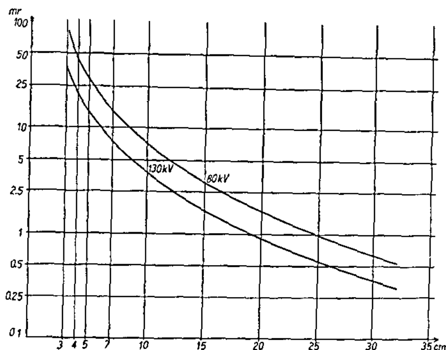


Fig 15 Gonad dose as a function of the distance of the field margin linear blurring in a direction parallel to the body axis Field size 18 × 24 cm subject thickness 20 cm pendulum angle 38 FFD 140 cm high kV extra fine grid of the ratio 12 5 1 The distance from field margin measured with the roentgen tube in centre position

with an increase in the lateral dose fall off in the upper layers of the phantom As regards scatter, on the other hand, the dose pattern varies from that of a stationary field in the case of a planigraph type equipment only when the section planes lie near the surface, and in the case of the polytome type when they lie at depths There is then an increase in the amount of scatter in the corresponding areas

Using unidimensional blurring, no appreciable variation in the dose is to be expected at right angles to the direction of tube travel during sectional radio graphy, and this point does not warrant any discussion

If, however, we compared the curves obtained with the Universal Planigraph and unidimensional blurring, with those from a polytome, using multidimen sional blurring (Fig 12), we see at once that the dose fall off in the latter is greater, which may be due to the shorter distance from tube to body surface The multidimensional movement of the tube moreover brings about a more even distribution of the dose over the area exposed to radiation, and this can be seen from the flatter curve with a steep fall off at the margins Since the exit dose is higher with polytome equipment than with the Universal Planigraph, by reason of the greater subject/film distance, the dose near the field is also higher

In parts removed from the field on the other hand, it approaches the values found with the Universal Planigraph As I see it, this can only be explained by the multidimensional blurring

The dose distribution at 130 kV, with the same filter (2 mm Al) as with 80 kV, is given in Fig 13 from which the substantial reduction in dose in parts of the phantom near the tube and the lower exit dose at the higher voltage may be seen The improved penetration power of the harder radiation is also apparent in the shortening of the dose curve On the other hand a relatively small decrease in radiation scatter is observed in areas both near and removed from the edges although (contrary to SEELENTAG's studies) there is here no absolute increase of dose with high kV radiation compared to that with softer rays This may be due to two circumstances firstly SEELENTAG based his values on a constant exit dose while the film dose was taken as the point of reference in this study so that depending on the grid used the exit dose at 130 kV was 37 % less than that at 80 kV, secondly the focus/surface distance is not the same If these factors are taken into account the results which match those of SCHAAL may be regarded as corroborative or complementary In Fig 14, values at 130 kV using the section technique are given Ignoring the variations in dose caused by the movement the same tendency as found under stationary field conditions remains

The loss of uniformity in dose distribution over the irradiated field which we found in section radiography as compared to a stationary field is thus the only difference between the two techniques There was at any rate no dose maximum in the phantom nor any dose concentration (as is encountered in moving field therapy) at the section depths investigated

III Gonad doses

The investigations on radiation scatter, outside the beam of rays and its dependence on the voltage finally lead to a consideration of doses received by the gonads in the course of various roentgen examinations An exhaustive treatment of this question is of course beyond the scope of the present paper, and we shall accordingly deal only with a few of the problems and those affecting stratigraphy in particular

Before discussing in detail the dose governing factors we must show how much radiation is in fact received by the gonads during section radiography of various organs The results obtained in measurements on patients during section radiography in our department over the last two years are summarized in Table 1 The measurements were made in men at points alongside the testicles and in women in the posterior vault of the vagina The values obtained for the men may be regarded as directly corresponding with the dose to the gonads whereas for the women they may only serve as an indication since the dose received in the vaginal vault may differ from that at the ovary,

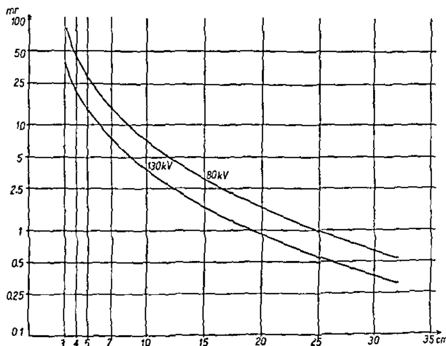


Fig 15 Gonad dose as a function of the distance of the field margin linear blurring in a direction parallel to the body axis Field size 18 × 24 cm subject thickness 20 cm pendulum angle 38 FFD 140 cm high kV extra fine grid of the ratio 12 5 1 The distance from field margin measured with the roentgen tube in centre position

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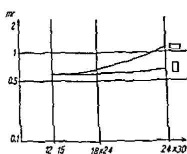


Fig 16 Gonad dose as a function of the field size at equal distances from field margin (*Universal Planigraph pendulum angle 38 radiographic kilovoltage 80 kV*)

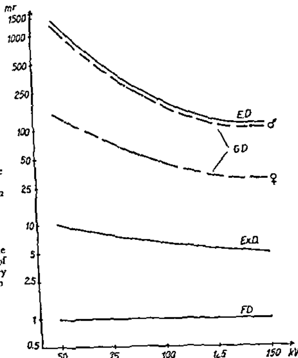


Fig 17 Gonad dose in radiography of the pelvis, male and female as a function of the radiographic kilovoltage Stationary field, FFD 140 cm field size 20 × 20 cm subject thickness 18 cm

Gonads positioned in the field.
E D — Incident dose
Ex. D — Exit dose
G D — Gonad dose
F D — Film dose

effect Increasing the size of the field from 15 to 24 cm brought about an increase in dose of approximately 20 % while increasing the field size to 30 cm brought the dose up by 75 % These figures too agree with those of HAYBITTLE and of MARTIN and EVANS observed under stationary field conditions

The effect of the voltage in exposures in which the gonads lie in the irradiated field is illustrated in Fig 17 Here again the patient was placed in a supine position *since this is used far more often than the prone at section radiography* It was found that for both testicles and ovaries the applied dose is reduced as the voltage increases As is evident from Fig 15 this also applies to the supine position *when the gonads are situated at some distance from the edge of the field* It will be seen from the dose curve for the ovaries that the reduction in dose obtained at depth with an increasing voltage is not nearly so striking *There is virtually no difference between the supine and prone positions in* women but in men the values obtained are on the whole lower in the prone position although with a grid the difference may be of the same order only as the *decrease in exit dose as compared to that behind the diaphragm* Pre filtration at the tube produces a decrease *in the dose to the gonads in men* in the supine position It has no effect whatsoever in the prone position, or to

Table 1

Doses received by the gonads in planigraphy of living patients

Organ	Dose per exposure in mr Mean value	Min	Max	Dose per examination in mr Mean value	Min	Max	80 % of all values per type of examination range between
Ear	0.03	0.007	0.12	0.57	0.007	1.32	0.1 — 0.75
Sinus	0.055	0.007	0.13	0.43	0.007	2.28	0.1 — 1.0
Apex of the lung	0.045	0.007	0.24	0.40	0.007	2.16	0.05— 0.90
Thoracic vertebr. a.p.	0.61	0.007	2.40	3.71	0.007	19.2	0.3 — 5.9
Thoracic vertebr. front	0.32	0.24	0.43	1.25	0.72	1.73	0.6 — 1.8
Gall bladder	0.37	0.03	0.78	1.58	0.12	3.36	0.3 — 2.3
Kidney	1.15	0.40	2.80	5.60	2.28	14.10	2.3 — 6.9
Lumbar vertebr. a.p.	5.5	0.42	27.0	12.03	1.68	135.0	2.5 — 50.0
Lumbar vertebr. front	4.57	0.41	19.80	19.3	1.64	156.6	2.0 —100.0
Lungs, without apices				1.71	0.18	6.84	0.2 — 4.8

according to the type of exposure being made, and as a result of anatomical variations. It has been shown by McGregor, however, that these values are of the same order of magnitude; using salpingography he found a mean difference of 1 : 1.4 between the dose in the posterior vaginal vault and the ovary.

The dose to the gonads increases steadily, from the cranium to the pelvic region, where it reaches levels of up to 27 mr per exposure. The range of values found show clearly that in none of the examinations were the gonads exposed to direct and unattenuated radiation. Despite the large material, it was not possible statistically to discover any unequivocal relationship between the various factors which in the separate measurements were found to be responsible for the size of the gonad dose. The major factors influencing the size of the gonad dose may therefore be shown by a few examples. As the most important of these factors we must cite the distance of the margin of the field from the gonads.

The dose values measured at the testicles of a supine patient at two kilo voltages, with craniocaudal movement of the tube, at a section plane in the centre of the body, are given in Fig. 15. The figures clearly show the considerable dose reduction when the distance is increased by only a few centimetres, especially when close to the gonads. An increase from 3 cm to 6 cm, for instance, brings about a 75 % reduction of the dose, while in areas remote from the gonads, increasing the distance from, say, 20 to 23 cm makes a difference of only 20 %.

The influence of the field dimensions is shown in Fig. 16. The size of the field was varied, while the distance between the borders of the field and the gonads was kept the same. The two curves show that in spite of the fact that blurring was along the craniocaudal axis the widening of the field produced the greater deflection, and that the length of the field apparently had very little

about 3 5 % of the overall number of exposures, the majority of these being of the lungs Section radiography of the bones and abdomen is of much smaller proportion In any case the examinations performed with the use of the sectional technique therefore mainly entail those in which the dose to the gonads is very small We can accordingly with confidence conclude that the somatic and genetic effects connected with section radiography, assuming of course technical competence in its performance, play no significant part in the exposure of man to ionizing radiation

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SUMMARY

The radiation dose at section radiography (tomography) has been determined by means of measurements on phantoms cadavers and living subjects Both in the area of direct radiation and in surrounding areas the dose with slightly varying distribution is of the same order as in survey radiography under identical conditions Dose requirements in both sectional and standard radiography are governed by the same rules The statistical assessment of the results of measurements of gonad doses in patients indicates that in a properly executed examination the radiation received during tomography makes only an insignificant contribution to the total radiation exposure of the population during diagnostic roentgen examinations.

ZUSAMMENFASSUNG

Auf Grund von Messungen an Phantomen an Leichen und am Lebenden wurde dosimetrisch die Strahlenbelastung bei Schichtaufnahmen bestimmt. Sowohl im direkt bestrahlten Gebiet als auch in dessen Umgebung liegt die Dosis bei etwas geanderter Verteilung etwa in derselben Grossenordnung wie bei Übersichtsaufnahmen unter gleichen Bedingungen Der Dosisbedarf unterliegt bei Schicht und Standardaufnahmen den gleichen Gesetzmassigkeiten Auch die statistische Auswertung der Messergebnisse der Gonadendosen am Patienten zeigt dass die mit der Schichtaufnahme verbundene Strahlenbelastung bei richtiger Durchfuhrung der Untersuchung die Gesamtbelastung der Bevolkerung durch rontgendiagnostische Massnahmen nur unwesentlich beeinflusst

RÉSUMÉ

La dose de rayonnement reçue au cours de la tomographie a été déterminée par des mesures sur des fantômes, sur des cadavres et sur des sujets vivants. Aussi bien dans la surface d ir radiation directe que dans les régions voisines, la dose reçue est du même ordre avec de petites différences de distribution que celle reçue pour une radiographie dans les memes

Table 2

Doses received by the gonads of the same patient in survey radiography and planigraphy of lungs and hip joint (FFD 150 cm, high kV extra fine grid, universal intensifying screens)

	Field size	Distance field edge to gonads	kV	mAs	Dose in mr
Survey radiography	35 × 35	23 cm	65	25	0 06
Planigraphic exposure	12 × 15	43 cm	65	60	0 04
	Hip joint (data as above)				
Survey radiography	30 × 40	3 cm	67	250	49 1
Planigraphic exposure,	18 × 24	9 cm	72	300	7 8
right hip joint	18 × 24	13 cm	78	300	4 15

the dose to the ovaries, since the effect of this filtration is entirely nullified in 10 cm of body tissue

A comparison between radiation doses received during a conventional roentgen examination and at sectional radiography is presented in Table 2 for radiography of the lungs of one and the same patient under identical conditions It may be seen that because the border of the field is closer to the gonads in the standard view of the lungs, and because the field is considerably larger, the dose to the gonads is practically the same despite the fact that the mAs value is *over 50 % lower than at section radiography* If the general view of the lungs is obtained without the grid (which was here a high kV extra fine grid, grid ratio 12 1) the dose is reduced by about 85 % The disadvantage of the planigraphic technique is evident, however, when we remember that a minimum of 4 to 6 exposures per examination will be involved, although even then the absolute dose level is still insignificant

If on the other hand we compare a general view of the pelvis with a sectional view of the hip joint, the immediate proximity of the gonads means that the smallness of the field (and the consequently greater gonad/field border distance) is greatly to the advantage of the section view, so much so, in fact, that 7 to 12 well masked section exposures are needed to make up the gonad dose from a single general view of the pelvis

If, finally, we consider to which extent section radiography under present conditions and henceforth may be justified we must bear in mind three important facts Firstly, sectional views are normally made only when the clinical and radiologic examinations have provided a sufficient indication Unlike the routine roentgen examinations section radiography is performed for a specific purpose and as such generally of great value both in diagnosis and therapy Secondly, they cover only part of the area included in survey radiography so that direct radiation is virtually never received by the gonads Thirdly, even in large hospitals with prodominantly clinical cases, this type of examination forms only a small part of the total, in our department the sectional views amount to

about 3 5 % of the overall number of exposures the majority of these being of the lungs Section radiography of the bones and abdomen is of much smaller proportion In any case the examinations performed with the use of the sectional technique therefore mainly entail those in which the dose to the gonads is very small We can accordingly *with confidence conclude that the somatic* and genetic effects connected with section radiography, assuming of course *technical competence in its performance play no* significant part in the exposure of man to ionizing radiation

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conditions Les regles fixant les doses admissibles sont les mêmes en tomographie qu en radiographie simple L étude statistique des résultats de mesures de doses gonades sur les malades indique qu avec un examen exécuté convenablement la dose reçue au cours de la tomographie ne contribue que de façon insignifiante à l irradiation totale reçue par la population du fait des examens radiologiques

REFERENCES

ARDRAN, G M und CROOKS H E *Gonad radiation* dose from diagnostic procedures Brit J Radiol 30 (1957), 295

BACKLUND, V Über die Technik der simultanen Telefilmplanigraphie Acta radiol (1956) Suppl 137

CEN, M and FRIK, W Raumdosis und Keimdrusendosis bei verschiedenen Strahlenqualitäten in der Rontgendiagnostik Fortschr Rontgenstr 88 (1958) 465

FRANKE H Die Norm im Rontgenbild Fortschr Rontgenstr 44 (1931) 691

GAJEWSKI H Physikalische und aufnahmetechnische Gesichtspunkte bei Rontgenaufnahmen mit hohen Spannungen Fortschr Rontgenstr 80 (1954), 642

— Grundlagen und Anwendungsmoglichkeiten des Simultan Schicht Verfahrens Rontgen u Lab Prax 9 (1956) 265

HAMMER JACOBSEN E Gonadedoser i diagnostisk radiologi (Danish) Ugeskr Laeg 119 (1957) 279

HARTUNG, K Zur Frage der Strahlenbelastung und des Strahlenschutzes in der padiatrischen Rontgendiagnostik Med Klin 53 (1958) 1209

HAYBITTLE J L The effect of field size on the dose of the patient in diagnostic radiology Brit J Radiol 30 (1957) 663

HERZ R H The spectral quantum and energy efficiency of calcium tungstate x ray intensifying screens Brit J appl Phys 7 (1956), 182

ICRP Report Exposure of man to ionizing radiation arising from medical procedures Phys in Med Biol 2 (1957) 107

ICRU Report Report of the International commission on Radiological Units and Measurements Handbook 62 U S Dept of Commerce N B S Washington D C 1956

JOHNS H E X rays and teleisotope γ rays *In* Hine and Brownell Radiation dosimetry, p 532 Academic Press New York 1956

KLOTZ E und SELLENTAG W Untersuchungen zur Belastung der Keimdrusen durch Hart strahldiagnostik Fortschr Rontgenstr 89 (1958), 92

LARSSON L E Radiation doses to the gonads of patients in Swedish roentgen diagnostics Acta radiol (1958) Suppl 157

LAUGHLIN J S and PULLMAN I Gonadal dose produced by the medical use of x rays *In* The biological effects of atomic radiation Nat Acad Sci Washington *D C 1957*

LIESS G Das Simultanschichtverfahren und seine Anwendung in der Rontgendiagnostik Dtsch Gesundheitsw 21 (1956) 693

MARTIN J H and EVANS A Radiation outside the defined field Brit J Radiol *32 (1959)* 7

MATTSSON O Practical photographic problems in radiography With special reference to high voltage technique Acta radiol (1955) Suppl 120

MOHR H Über Messung der Gonadendosis bei Patienten in der Rontgendiagnostik Strahlen ther 106 (1958) 80

MORGAN R H The control of diagnostic quality in roentgenograms of the chest Amer J Roentgenol 50 (1943), 149

OSBORN S B and SMITH, E E The genetically significant radiation dose from the diagnostic use of x rays *in* England and Wales Lancet 1956 I p 949

SCHAAL, A Beitrag zur Frage der Streustrahlenbelastung des Patienten bei Rohrenspannungen von 60 bis 180 kV Fortschr Rontgenstr 90 (1959) 247

SCHOBER H Die Abhangigkeit der Durchschnittsschwarzung bei Rontgenbildern vom gewahlten Format und von der gestellten Aufgabe Vortrag IX. Internat Congr f Radiologie in Munchen 1959

SEELENTAG W Zur Frage der genetischen Belastung der Bevolkerung durch die Anwendung ionisierender Strahlen in der Medizin Teil I bis IV Strahlenther 104 (1957) 182 105 (1958) 169 107 (1958) 337 537

— *und* KLOTZ E. *Die Streustrahlung im Korper bei Strahlenqualitaten von 50 bis 200 kV* Erzeugerspannung Strahlenther 108 (1959) 112

SIEVERT R Eine Methode zur Messung von Rontgen Radium und Ultrastrahlen nebst einigen Untersuchungen uber die Anwendbarkeit derselben in Physik und Medizin Acta radiol (1932) Suppl 14

SORRENTINO J and YALOW R A nomogram for dose determinations in diagnostic roentgenology Radiology 50 (1950) 748

SPIEGLER, G Das Rontgenbild — dosimetrisch betrachtet Fortschr Rontgenstr 80 (1954) 754

STANFORD R W The use of cones and filters to reduce patient dosage in diagnostic radiology Brit. J Radiol 30 (1957) 497

STIEVE F E Untersuchungen uber das Wirkungsprinzip von Belichtungsautomaten fur Rontgenaufnahmen Fortschr Rontgenstr 85 (1956) 491

THE HAZARD TO MAN OF NUCLEAR AND ALLIED RADIATION British Medical Research Council London 1956

WACHSMANN F Dosisbelastung des Patienten bei rontgenologischen Untersuchungen Fortschr Rontgenstr 75 (1951) 728

— BREUER K und BUCHHEIM E Grundlagen und Ergebnisse der Hartstrahltechnik. Fortschr Rontgenstr 76 (1952) 147

WIDENMANN L Untersuchungen uber die Abhangigkeit der Filmschwarzung mit handelsublichen Verstarkerfolien von der Strahlenqualitat Fortschr Rontgenstr 87 (1957) 386

— Vergleichende Untersuchungen über Bildqualitat und Dosisbedarf bei Simultan und Einzelschichtaufnahmen Fortschr Rontgenstr 89 (1958) 613

WILSLEY R B The intensity of scattered x rays in radiography Amer J Roentgenol 8 *(1921)* 328

ZIELER E Aquivalente Aufnahmebedingungen in der Rontgendiagnostik Acta radiol 43 (1955) 393

FROM THE BIOLOGY LABORATORY, HANFORD RESEARCH LABORATORIES, RICHLAND, WASHINGTON, U S A

BEHAVIOR OF I^{131} FOLLOWING ITS INHALATION AS A VAPOR AND AS A PARTICLE

by

D H WILLARD and W J BAIR

One of the potential hazards associated with certain atomic energy facilities is the release of I^{131} to the atmosphere from a reactor or during the separation of plutonium from fission products and uranium Considerable effort has been expended to define the hazards of ingested I^{131} (BUSTAD et coll 1957) but few data are available on the entry of I^{131} into the body by breathing air containing I^{131} either as a vapor or as a particle Because of the extreme solubility of I^{131} vapor, it is usually assumed that whether I^{131} enters the blood through the lungs or through the gastrointestinal tract, its behavior and effects will be the same If inhaled as an insoluble particle it would be expected that I^{131} would tend to remain in the lung longer and not be translocated immediately to thyroid tissue However, for purposes of establishing maximum permissible limits, it is helpful to have experimentally determined deposition, retention, and translocation data This paper reports data obtained using mice and sheep breathing air containing very soluble I^{131} vapor and air containing 'insoluble' AgI^{131} particles Iodine vapor is known to be rapidly absorbed by animal tissues, and silver iodide is one of the most water-insoluble iodine compounds

Work performed under Contract No AT(45-1) 1350 between the Atomic Energy Commission and the General Electric Company Submitted for publication 7 November 1960

Table 1

Experimental design of exposures

	Number of animals	Inhalation Exposure time (minutes)	Aerosol concentration ($\mu C/cc$)	Additional routes of administration Number of animals	Route
I_2^{131}	80 mice	30	2.3×10^{-3}	—	—
	3 sheep	20	1.0×10^{-3}	—	—
NaI^{131}	—	—	—	1 sheep	Intragastric
AgI^{131}	80 mice	120	3.0×10^{-3}	1 sheep	Intragastric
	3 sheep	30	7.8×10^{-3}	1 sheep	Subcutaneous
				1 sheep	Intraperitoneal

Methods

Mouse exposures The experimental design is given in Table 1 Eighty two-month-old female BAF mice obtained from the Jackson Memorial Laboratory were exposed to I^{131} vapor and 80 were exposed to an aerosol of AgI particles Immediately following exposure and at intervals up to 90 hours after exposure groups of 10 mice were killed for radiochemical assay of all tissues The tissues were digested with a 0 25 N sodium hydroxide solution and aliquots were plated and counted with an end window Geiger Muller tube The method for exposing mice to radioactive aerosols was described in detail by WILLARD et coll (1958) Briefly mice were individually placed head first in 50 ml conical centrifuge tubes with the bottom one half inch (12 6 mm) removed to give a three eighths inch (9 5 mm) opening The tubes plugged with tissue paper and stoppered were inserted into ports drilled into the side of a verticle exposure chamber constructed of 16 inches (407 mm) of 8 inch (204 mm) (O D) lucite pipe The chamber held 84 tubes in 7 rows of 12 each The aerosol was admitted at the top and exhausted at the bottom through a 0 5 N sodium hydroxide scrubber to remove I^{131} vapor and through an electrostatic precipitator to remove AgI^{131} particles before the air was exhausted from the building Samples of the aerosol in the chamber were collected by pulling known quantities of air through four small sodium hydroxide scrubbers for I^{131} vapor or through four millipore filters (type AA manufactured by the Millipore Filter Corporation) for AgI^{131} particles Radiochemical assay of the scrubbers and filters gave the average concentration of I^{131} in the chamber during the exposure period Fig 1 is a photograph of the exposure chamber within a glove box

Sheep exposures Six nine month old purebred male Suffolk sheep weighing 60 to 70 kilograms were used in this experiment Their diet consisted of chopped alfalfa and a grain mixture fed twice daily (BUSTAD 1952) The sheep were kept in metabolism cages and were monitored by duplicate neck counts with complete repositioning of collar each time the animal was monitored A thyroid monitoring device specifically designed for sheep was used to detect the gamma radiation emanating from the gland region (HERDE et coll 1952) Background count was determined by placing the monitoring instrument on the rump of the animals

Sheep were exposed by a method similar to that used for mice except that the I^{131} aerosol was drawn into a plastic bag which was contained in a round cardboard shipping crate 28 inches (712 mm) in diameter A mask was attached to the bag through a lucite cover on the container with a one inch (2 54 mm) pipe fitting and a three way valve Sheep inhaled the aerosol from the bag and exhaled into a sodium hydroxide trap

Parenteral injections were made using a 10 ml syringe fitted with a 22 gage needle the

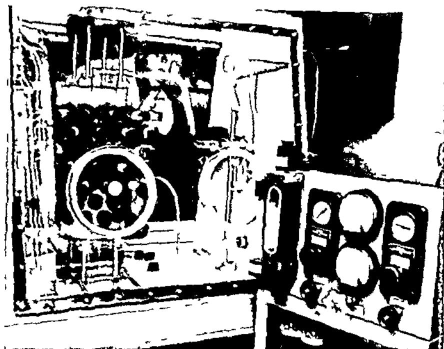


Fig 1 Mouse exposure chamber within a glove box

intraperitoneal injection being given in the paralumbar fossa and the subcutaneous injection given in the inguinal region Oral administrations were made by feeding sheep food pellets containing NaI^{131}

Generation of iodine vapor Iodine vapor was generated by the method of DAILEY (1945) and modified by SELDERS (1956) All glassware and the exposure chamber were treated with dri film (dimethyldichlorsilane General Electric Company) A generator was fashioned from a 100 ml test tube Fig 2 Four ml H_2O 1 25 ml NaI^{131} (14 3 mC — purchased from the Oak Ridge National Laboratory) 6 g $FeSO_4$ and 0 5 ml H_2SO_4 were placed in the generator With the generator connected to the exposure chamber and 500 cc air per minute being bubbled through the mixture in the generator one ml H_2O_2 was added to start the release of iodine vapor After 30 minutes the reaction was stopped by the addition of one millilitre saturated sodium bisulfide

AgI^{131} particles AgI^{131} particles were prepared by adding 2 mg of I as NaI 1 25 ml NaI^{131} (15 57 mC) and 0 1 ml 0 1 N $AgNO_3$ to 23 ml H_2O in a 125 Erlenmeyer flask on a magnetic stirrer After being stirred for 15 minutes at room temperature the suspension was filtered through a millipore filter After addition of 0 1 ml $AgNO_3$ the filtrate was stirred for one hour longer then filtered through the same millipore filter The filtrate was discarded and the filter containing the precipitate was placed in a 50 ml conical centrifuge tube The millipore filter was dissolved by washing and centrifuging twice with 3 ml acetone The precipitate was then washed with water and suspended in 20 ml of 0 1 per cent aqueous polypropyleneglycolethylene oxide polymer (Wyandotte Chemical Company) solution Before transfer to the aerosol generator the particles were placed on an ultrasonic generator for several hours to break up aggregates The solubility of AgI^{131} prepared in this manner was 2 per cent in H_2O and 34 per cent in Ringer s solution at 37 C The generator used to

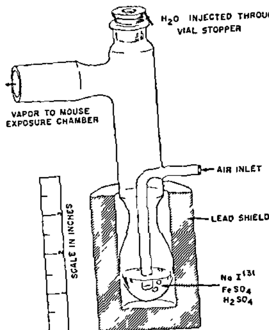


Fig 2 I apor generator

atomize AgI^{131} particles from the Pluronics suspension was described by WILLARD et coll (1958) With this generator dispersal of the particles in a fog was effected by forcing air at 20 psi through an orifice (No 80 size hole) in the side of a 12 gage spinal needle at the end and inserted into the suspension to a level placing the orifice just above the surface of the suspension The fog was then passed into the exposure chamber The particles collected on millipore filters from the exposure chamber were sized by electron microscope examination. The mean size was about 0 25 m crons by count

Results

Mouse experiments — I^{131} vapor The average concentration of I^{131} in the chamber during the 30 minute exposure period was $2\,2 \times 10^{-3}$ μC/cc air It was assumed that mice inhaled an average of 25 cc air per minute (WADC Technical Report 1956 and GUYTON 1947) A similar tidal volume was observed in this laboratory It was estimated then that 16 μC of I^{131} were inhaled by each mouse About 60 per cent of this was deposited in the mouse and the remainder apparently exhaled The distribution of I^{131} vapor in the mouse is given in Fig 3 The per cent of the I^{131} inhaled that was present in each tissue is shown as a function of time after exposure The rapid initial transfer of I^{131} to the circulatory system not only from the lung but from the upper respiratory and the gastrointestinal tracts is indicated by the high

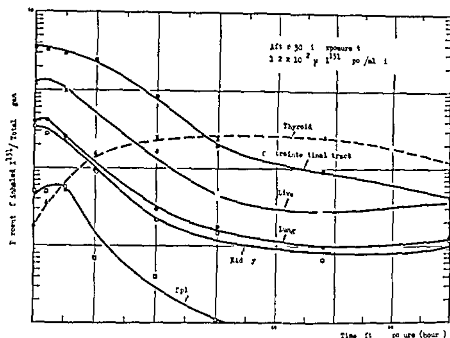


Fig 3 Distribution of I^{131} in mice after inhalation of I^{131} vapor After 30 min exposure to 1.2×10^{-2} μC I^{131} vapor/cc air

percentages present in liver, kidney, and spleen As the level in these tissues and in lung and gastrointestinal tract decreased, the quantity in thyroid increased The maximum level in the thyroid was 0 4 μC and occurred about 30 hours after exposure This was about 2 5 per cent of the total quantity of I^{131} or about 4 per cent of the total deposited Forty eight hours after exposure the quantity in thyroid began to decrease The apparent clearance of I^{131} from lung (half time of two to four hours) is in reality probably the rate of clearance of I^{131} from blood because similar clearance rates were observed for liver, kidney, and gastrointestinal tract The actual clearance from lung was undoubtedly almost instantaneous

AgI^{131} particles The average concentration of AgI^{131} in the chamber during the two hour exposure period was 3×10^{-3} μC/cc of air The total quantity inhaled per mouse, assuming an average of 25 cc of air breathed per minute, was 9 μC Of this only about one μC or 12 per cent was deposited and the remainder probably exhaled The distribution of I^{131} in the mouse after inhalation of AgI^{131} particles is shown in Fig 4 About 2 per cent of the total quantity breathed was in the lung at the end of the exposure period, about 6 per cent in the gastrointestinal tract and 2 per cent in liver Again the rapid transfer of I^{131} to blood was indicated by the early presence in spleen, kidney, adrenals, and liver The apparent four to six hours half time required for clearance of I^{131} from the lung was again probably the clearance of I^{131} from

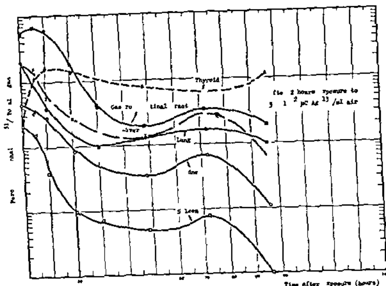


Fig 4 Distribution of I after inhalation of AgI[11] After 2 hrs exposure to 3 × 10⁻ μC AgI[3]/cc air

blood The maximum level in thyroid was attained after 10 hours and was about 2 per cent of the total quantity inhaled

For comparison of the distribution of I^{131} in tissues after inhalation of I^{131} vapor with distribution after inhalation of AgI^{131} particles the percentage of the total body burden per tissue is plotted against time in Fig 5 In these calculations the eviscerated carcass was excluded to eliminate errors due to surface contamination of the fur Data for spleen adrenals and ovaries are not included because these organs contained a relatively small per cent of the total I^{131} The maximum amount in the thyroid was 60 per cent of the body burden and occurred about 50 hours after inhalation of either I^{131} vapor or insoluble AgI particles

Sheep experiments Three sheep were exposed to I^{131} vapor and three to AgI^{131} particles via the respiratory route The total microcuries of I^{131} inhaled (but not necessarily deposited) were estimated from the concentration in the chamber the duration of the exposure and the average minute volume determined during many pre I^{131} exposure test runs The I^{131} inhaled varied from 180 to 290 μC for three sheep (Table 2) The quantity of I^{131} present in the thyroid at the time of maximum uptake (20 to 35 hours after exposure) varied from 3 to about 8 per cent of the total inhaled The AgI^{131} data for sheep were less certain Due to difficulties encountered in the collection of aerosol samples estimates of the I^{131} inhaled as AgI^{131} particles may be in

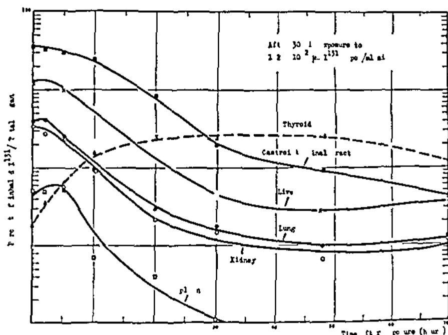


Fig 3 Distribution of I^{131} in mice after inhalation of I^{131} vapor After 30 min exposure to 1.2×10^{-2} μC I^{131} vapor/cc air

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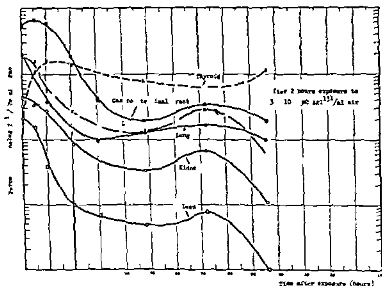


Fig 4 Distribution of I' after inhalation of AgI After 2 hrs exposure to 3 x 10⁻ μC AgI '/cc air

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For comparison of the distribution of I^{131} in tissues after inhalation of I^{131} vapor with *distribution after inhalation of* AgI^{131} particles, the percentage of the total body burden per tissue is plotted against time in Fig 5 In these calculations the eviscerated carcass was excluded to eliminate errors due to surface contamination of the fur Data for spleen, adrenals and ovaries are not included because these organs contained a relatively small per cent of the total I^{131} The maximum amount in the thyroid was 60 per cent of the body burden and occurred about 50 hours after inhalation of either I^{131} vapor or insoluble AgI particles

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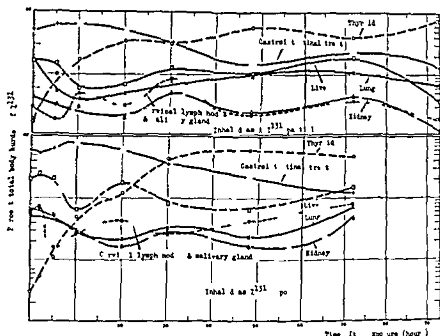


Fig 5 Distribution of I^{131} in the mouse after inhalation of AgI^{131} particles

error In one sheep, about 2 per cent of the I^{131} inhaled was in the thyroid 20 hours after exposure The time of maximum uptake by thyroid varied from 20 to 24 hours, which was less than when I^{131} vapor was inhaled

To test the relative behavior of 'soluble and 'insoluble' forms of I^{131}, NaI^{131} was given orally, and AgI^{131} was given orally, subcutaneously, and intra peritoneally to four of the same sheep used in inhalation experiments In all of these, the time for maximum uptake (40 to 60 per cent of the I^{131} given) in thyroid was 28 to 34 hours The biological half life was four and one half to seven days, and except for one sheep, was about the same that was observed after inhalation

Discussion

Dailey (1945), using anesthetized rats breathing I^{131} through tubes inserted into the tracheas, found that 10 per cent of the inhaled I^{131} was deposited during a 30 minute exposure Of that deposited, only 5 per cent was in the lung of rats killed immediately after the exposure In this study, where the exposure was not confined to the lungs, about 60 per cent of the I^{131} inhaled was deposited after a 30 minute exposure Only about 4 per cent of that inhaled was in the lungs This was about 7 per cent of the whole body burden, or of the total amount retained

Dailey also found that the thyroid reached a maximum of about 10 per cent of the deposited dose of I^{131} after 48 hours In the present study with

Table 2

Thyroid uptake of I^{131} in sheep

Sheep number	Thyroid weight* (grams)	Aerosol	By inhalation ** μC I^{131} inhaled	Maximum μC I in thyroid	Time of maximum (hours)	Per cent of inhaled	Biological half life (days)	By other routes I^{131} compound and route of admin	μC I given	Maximum μC I^{131} in thyroid	Time of maximum (hours)	Per cent of dose	Biological half life (days)
6	7 4	I^{131}	180	7 3	20	4 1	4-1/2	NaI^{131} (oral)	25	14	28	56	4 1/2
7	4 9	I^{131}	290	22	35	7 5	6-1/2	—					
27	6 6	I^{131}	260	7 5	35	2 9	4-1/2	AgI^{131} (oral)	46	22	34	48	6-1/2
5	3 4	AgI^{131}	9 6***	6 4	20	?	6-1/2	—					
696	7 0	AgI^{131}	610***	10	20	1 7	4 1/2	AgI^{131} (Sub-Q)	46	19	28	41	4-1/2
697	8 5	AgI^{131}	24***	7 4	24	?	6-1/2	AgI^{131} (I P)	46	22	34	47	7

* At conclusion of the experiment

** Aerosol concentrations were 1×10^{-3} μC/cc I^{131} vapor and $7\ 8 \times 10^{-3}$ μC AgI^{131} particles

*** These values may be in error due to difficulties in collecting representative samples of the aerosols

mice the level of I^{131} in the thyroid reached a maximum of 4 per cent of the deposited dose after 30 hours In view of the many factors which affect thyroid uptake of iodine one of the most important being the total iodine content of the diet the results of the two studies are not in marked disagreement No attempt to control the iodine intake via the diet was made in either study, although it was known that the daily iodine intake for sheep was 0 3 to 0 5 mg DAILEY administered I^{131} by intratracheal tube thus limiting the area of absorption to tracheal and pulmonary tissue The absorption of I^{131} may be more rapid and more complete in pulmonary tissues than in the upper respiratory and gastrointestinal tract In this study a large fraction of the I^{131} was deposited in the upper respiratory passages and gastrointestinal tract. This might account for the absorption as being less than reported by DAILEY As in this study DAILEY found the apparent clearance rate of I^{131} from lung to be almost identical to that from the rest of the carcass and concluded that the observed lung activity was really blood activity In both of these inhalation studies the percentage of I^{131} reaching the thyroid was lower than the 15 to 80 per cent reported after other routes of administration (BUSTAD et coll 1957)

The values estimated for the total quantity of I^{131} inhaled but not necessarily deposited can reflect several possible errors These include the assumed value for the minute volume and the measurement of the average concen

tration of I^{131} in the inhaled air It is unlikely, however, that the estimated percentage of inhaled I^{131} that was accumulated in the thyroid following inhalation of I^{131} vapor (2 5 per cent in mice and 3 to 7 5 per cent in sheep) was in error more than a factor of two The total deposition of inhaled AgI^{131} particles (12 per cent in mice), however, was considerably lower than the 60 to 80 per cent observed in mice after inhalation of $Pu^{239}O_2$ or $Ru^{106}O_2$ (BAIR 1960) Neglecting the possibility of errors occurring in collecting and counting the AgI^{131} particles or in the assumed minute volume, the difference may be due to particle shape The mean diameter of particles was between 0 2 and 0 3 microns which was comparable to the $Ru^{106}O_2$ and $Pu^{239}O_2$ Under electron microscopic examination the AgI^{131} particles appeared as small spheres $Ru^{106}O_2$ particles were three dimensional chain aggregates and $Pu^{239}O_2$ particles were aggregates of cubes

The results with sheep were in general agreement with those with mice Maximum thyroid uptake of I^{131} occurred sooner after exposure to AgI^{131} (10 hours in mice and 20 to 24 hours in sheep) than for I^{131} vapor (30 hours in mice and up to 35 hours in sheep)

The biological half lives for iodine in the thyroids of the nine month old sheep used in this study ranged from four and one half to seven days Values of 14 to 46 days were observed in earlier studies in which ten month old sheep were fed food pellets containing I^{131} (HEALY et coll 1957) The reason for this difference is unknown since dietary iodine levels were the same for the sheep used in both studies It was unexpected that the translocation from the site of injection of both subcutaneous and intraperitoneal particles would be as rapid as from inhaled or ingested vapors or particles This rapid translocation further emphasizes the unusual properties of the body fluids in the solubilization of inert particles and their immediate transport to specific organs or tissues The apparent tissue solubility of AgI was unexpected even though the solubility of AgI used in these experiments was 2 per cent in H_2O and 34 per cent in Ringer's solution After inhalation there was little difference between the absorption of I^{131} administered as a gas and as silver iodide particles Similar rapid translocation was observed following introduction of $Sr^{90}SO_4$ into dog's lung (SMITH et coll 1959) However, $SrSO_4$ is much more soluble in water and acids than is AgI These results also emphasize the unusual properties of body fluids and show that one cannot always predict what will occur in body tissues on the basis of tests with pure solvents alone

Conclusions

These studies confirmed the often observed rapid absorption of I^{131} by tissue, occurring even when given in a relatively insoluble form, AgI In mice at least 60 per cent of the inhaled I^{131} vapor was deposited Twenty to 40 hours later the thyroid contained 2 5 per cent of the total inhaled This may

have been as high as 7 5 per cent in sheep These results are not in complete agreement with the data tabulated by the International Commission on Radiological Protection (1959) Seventy five per cent of the quantity inhaled is expected to be deposited in the whole body and 23 per cent will be trans located to thyroid tissue

Acknowledgements

The authors wish to express their appreciation to Mr ARTHUR CASE of the Biological Analyses Operation for I^{131} counting of tissue samples to Mr WOODROW LEACH of the Technical Shops Operation for fabrication of the special glassware and to Dr LEO K BUSTAD of the Experimental Animal Farm for encouragement and advice The authors are particularly indebted to Mr L A TEMPLE and Mr M G BROWN of the Pharmacology Operation to Capt. G D SMITH (USAF VC) (Air Force veterinarian formerly assigned to the Biology Operation) and to members of the Experimental Animal Farm staff for their assistance with the experiments

SUMMARY

In mice the maximum thyroid uptake occurred 20 to 30 hours after inhalation of I^{131} 2.5 per cent of total I^{131} inhaled as vapor and 1 6 per cent of the total inhaled as insoluble AgI^{131} This amount represented 60 per cent of the total body burden In sheep the maximum thyroid uptake occurred between 20 and 35 hours after inhalation oral subcutaneous or intraperitoneal administration Two to 7 per cent of inhaled I^{131} appeared in thyroid com pared with 40 and 60 per cent of that given by other routes The results with inhaled AgI^{131} particles emphasize the unusual properties of the body fluids in solubilizing relatively in soluble particles

ZUSAMMENFASSUNG

Bei Mausen trat die maximale Aufnahme in der Schilddruse 20—30 Stunden nach Inhala tion von J^{131} auf 2 5 des totalen J^{131} wurde als Gas inhaliert und 1 6 % der gesamten Jod menge wurde als unlosliches AgJ^{131} inhaliert Diese Ziffern representierten 60 % der Totalbestrahlung Bei Schafen trat die maximale Aufnahme in der Thyreoidea nach Inhala tion, oraler subkutaner oder intraperitonealer Administrierung nach 20—35 Stunden auf 2 % —7 des inhalierten J^{131} erschienen in der Thyreoidea verglichen mit 40—60 % des auf andere Weise administrierten Jodes Die Ergebnisse mit inhalierten AgJ^{131} Partikeln zeigen deutlich die ungewohnlichen Eigenschaften der Korperflussigkeiten auf relativ un losliche Partikel auflosen zu konnen

RÉSUMÉ

La fixation thyroïdienne maximale se produit chez des souris entre 20 et 30 heures après l'inhalation de I^{131} 2 5 pour cent du total de I^{131} inhalé sous forme de vapeur et 1 6 pour cent du total de I^{131} inhalé sous forme de AgI^{131} insoluble Cette quantité représente 60 pour cent de la quantité corporelle totale Chez des moutons la fixation thyroïdienne maxi male se produit entre 20 et 35 heures après inhalation ou administration orale, sous-cutanée ou intrapéritonéale La quantité de I^{131} inhalé fixée par la thyroïde est de 2 à 7 pour cent alors qu'elle est de 40 à 60 pour cent pour l'iode administré par les autres voies. Les résultats obtenus avec les particules de AgI^{131} montrent que les liquides organiques ont des propriétés inhabituelles pour solubiliser des particules relativement insolubles

REFERENCES

BAIR, W J Deposition, retention translocation and excretion of radioactive particles *In* Inhaled particles and vapors Pergamon Press Oxford In press

BUSTAD, L K, WARNER, D E and KORNBERG, H A Effect of stable iodine on uptake of radioiodine in sheep Amer J vet Res 19 (1958), 883

— GEORGE Jr L A, MARKS, S et coll Biological effects of I^{131} continuously administered to sheep Rad Res 6 (1957) 380

— HERDE K L, WARNER, D E and KORNBERG H A Toxicity of I^{131} in sheep I General (Preliminary report on low level chronic effects) Hanford Biology Research — Annual Rep 1951, Document HW 25021 (1952), 139

DAILEY, M, WENDER, I and ABRAMS, R Tracer studies with inhaled eight day iodine Terminal Rep Chicago Univ metallurg Lab Document MDDC 251 (1945)

GUYTON, A C Measurement of the respiratory volumes of laboratory animals Amer J Physiol 150 (1947) 70

HANDBOOK OF BIOLOGICAL DATA I dit by W S Spector Saunders Philadelphia 1956

HEALY J W CLARKE, W J SEIGNEUR L J et coll Early uptake of radioiodine in the thyroid of the sheep Hanford Biology Research — Annual Rep 1957 Document HW 53500 (1958), 75

HERDE, K W, WARNER, D E and BUSTAD L K Toxicity of I^{131} in sheep II Instrumentation Hanford Biology Research — Annual Rep 1951, Document HW 25021 (1952), 160

Recommendations of the International Commission on Radiological Protection Report of Committee II on Permissible Dose for Internal Radiation (1959) 193

SELDERS A A and HUNGATE F P The foliar sorption of iodine by plants Hanford Atomic Products Operation Document HW 44890 (1956)

SMITH, G D and BAIR, W J Aerosol exposure through a surgically prepared tracheal fistula Hanford Biology Research — Annual Rep 1958, Document HW 59500 (1959) 97

WILLARD D H BAIR W J, TEMPLE L A and SMITH, V H Techniques for exposure of mice to aerosols of radioactive particles Hanford Atomic Products Operation Document HW 52368 (1958)

Subject Index to Volume 55

ROENTGEN DIAGNOSIS

Nervous system

Digestive tract

Heart and Vessels (incl lymphatic vessels)

Lungs Pleura, Mediastinum and Chest walls

Bones and Joints

Uro-Genital system

RADIOACTIVE ISOTOPES

RADIOPHYSICS

TECHNIQUE

Roentgen examinations

Contrast media

Radiotherapy

BOOK REVIEWS

List of Authors

(r) indicates 'reviewed only'